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DOCKET NO.: 18-971-0 PCT

DIRECTOR OF THE UNITED STATES
PATENT AND TRADEMARK OFFICE
ALEXANDRIA, VIRGINIA 22313

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STEPHEN G. BAXTER
(703) 413-3000
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RE: Patent No.: 6,107,458
Serial No.: 08/809,723
Patentees: Hidenori OHKI et al
Issue Date: August 22, 2000
For: CYCLIC HEXAPEPTIDES HAVING ANTIBIOTIC ACTIVITY

SIR:

Attached hereto for filing are the following papers:

REQUEST FOR CERTIFICATE OF CORRECTION; CERTIFICATE OF CORRECTION (IN DUPLICATE, 3 PP.); PHOTOCOPY OF ORIGINAL CLAIMS OF SPECIFICATION AS FILED 05/21/97; PHOTOCOPY OF OFFICE ACTION MAILED 08/28/97; PHOTOCOPY OF U.S. 5,376,634; PHOTOCOPY OF OFFICE ACTION MAILED 06/15/98; PHOTOCOPY OF AMENDMENT PURSUANT TO 37 C.F.R. §1.116 FILED 12/07/98; PHOTOCOPY OF PRELIMINARY AMENDMENT FILED 02/08/99

Our credit card payment form in the amount of $100.00 is attached covering any required fees. In the event any variance exists between the amount enclosed and the Patent Office charges for filing the above-noted documents, including any fees required under 37 C.F.R §1.136 for any necessary Extension of Time to make the filing of the attached documents timely, please charge or credit the difference to our Deposit Account No. 15-0030. Further, if these papers are not considered timely filed, then a petition is hereby made under 37 C.F.R. §1.136 for the necessary extension of time. A duplicate copy of this sheet is enclosed.

Respectfully submitted,

OBLON, SPIVAK, McCLELLAND,
MAIER & NEUSTADT, P.C.

Stephen G. Baxter
Attorney of Record
Registration No. 32884

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Vincent K. Shier, Ph. D.
Registration Number 50,552

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

IN RE PATENT OF: :
Hidenori OHKI et al :

PATENT NO.: 6,107,458 :

ISSUED: August 22, 2000 :

FOR: CYCLIC HEXAPEPTIDES HAVING ANTIBIOTIC ACTIVITY

REQUEST FOR CERTIFICATE OF CORRECTION

DIRECTOR OF THE UNITED STATES PATENT AND TRADEMARK OFFICE
ALEXANDRIA, VA 22313-

SIR:

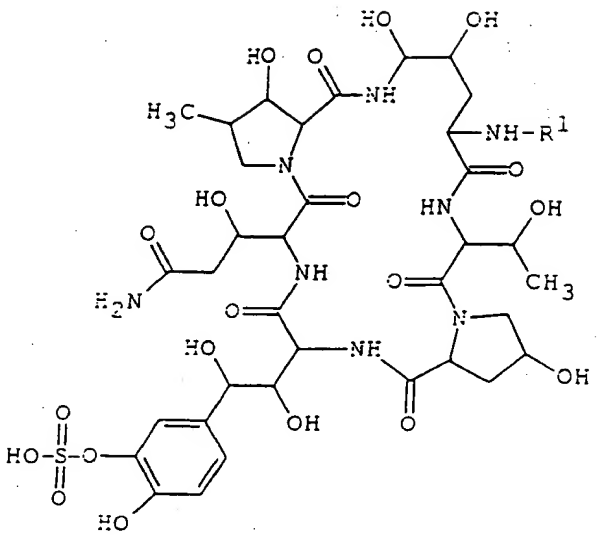
The following is a request for a Certificate of Correction in U.S. Patent Application Serial Number 08/809,723, now U.S. Patent Number 6,107,458.

REMARKS

A Certificate of Correction under 35 U.S.C. §255 is respectfully requested, in U.S. Patent Number 6,107,458 ("the '458 patent"). The facts are as follows.

The '458 patent issued from U.S. Patent Application Serial Number 08/809,723 ("the '723 application"), which was a 371 application of PCT/JP95/01983, filed on September 29, 1995. The '723 application entered the national stage in the U.S. on April 27, 1997, and the requirements of 35 U.S.C. § 371 were completed on May 21, 1997.

The '723 application was filed with 19 original claims, a copy of which is attached hereto at Tab 1. Notably, as shown by the formula [I] in Claim 1, the '723 application is directed toward certain cyclic hexapeptides. For convenience, formula [I] is repeated below:

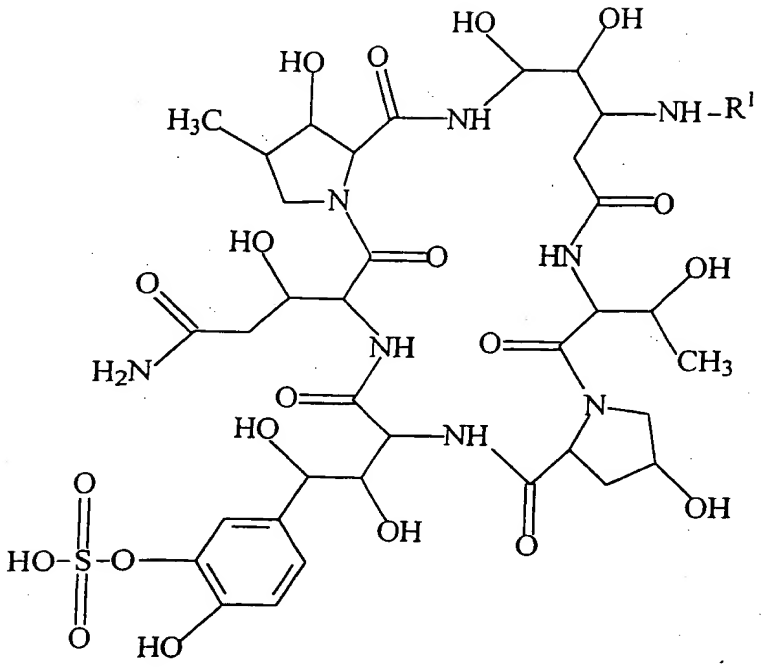


[I]

It is also noted that the structure of formula [I] in originally presented Claim 1 is fully supported by the specification of both the '723 application, as originally filed, and the '458 patent, as issued. In support of this assertion, Applicants cite page 2 of the '723 application, as originally filed, and col. 1 of the '458 patent.

In the Office Action dated August 28, 1997, Claims 1-19 were rejected under 35 U.S.C. § 103(a) in view of, *inter alia*, U.S. Patent No. 5,376,634 (Iwamoto et al.). For convenience, copies of the Office Action dated August 28, 1997, and Iwamoto et al. are attached hereto at Tabs 2 and 3. In the Request for Reconsideration filed on March 2, 1998, no amendments were made to the claims other than the cancellation of Claims 17 and 18.

In the Office Action dated June 5, 1998, Claims 1-16 were finally rejected in view of Iwamoto et al. (copy attached hereto at Tab 4). In response, Applicants canceled Claims 1-16 and added new Claims 20-36 (*see*, copy of the Amendment Pursuant to 37 C.F.R. §1.116, filed on December 7, 1998, a copy of which is attached hereto at Tab 5). However, a typographical error was introduced into the structure for formula [I] in Claims 20, 23, 28, 29, and 30 and the structure for formula [II] in Claims 29 and 30. Specifically, the position of the attachment of the $-NH-R^1$ group was inadvertently moved by one position on the main ring as shown below:



[I]

Inspection of the remarks, which accompanied the Amendment, makes it clear that the shift of the position of the attachment of the $-NH-R^1$ group on the main ring was merely an inadvertent typographical error. Specifically, there is nothing in the remarks which accompanied the Amendment which would in anyway indicated that this shift in position was intentional.

In the Advisory Action dated December 21, 1998, the Examiner indicated that the amendment filed on December 7, 1998, would not be entered. Applicants then re-filed the '723 application as a CPA along with a Preliminary Amendment in which Claims 20-36 were replaced with Claims 37-41 (*see*, copy of the Preliminary Amendment, filed on February 8, 1999, a copy of which is attached hereto at Tab 6). However, the typographical error in the structure of formula [I] (and in the structure of formula [II]) which was introduced in the Amendment filed on December 7, 1998, was propagated in the Preliminary Amendment filed on February 8, 1999.

Once again, inspection of the remarks which accompanied the Preliminary Amendment filed on February 8, 1999, shows that the shift of the position of the attachment of the $-NH-R^1$ group on the main ring was merely a propagation of the inadvertent typographical error which had been previously introduced. Moreover, the fact that the Examiner then allowed the application

indicates that this typographical error simply went unnoticed and that the Examiner had intended to allow those claims with the correct structure.

In other words, the entire prosecution history points to the conclusion that the mistake in the structure of formulae [I] and [II] is simply a typographical error which went unnoticed during prosecution. Further, there is no evidence that this error was introduced in bad faith.

As stated in 35 U.S.C. § 255:

> Whenever a mistake of a clerical or ***typographical*** nature, or of a minor character, which was not the fault of the Patent and Trademark Office, appears in a patent and a showing has been made that such mistake occurred in ***good faith***, the Director may upon payment of the required fee, issue a certificate of correction, if the correction does not involve such changes in the patent as would constitute ***new matter*** or would require ***re-examination***.

As can be seen from the facts set out above, this particular instance meets all the requirements for the issuance of a certificate of correction. Specifically, the error in the structure of formulae [I] and [II]:

(1) is a typographical error; and

(2) occurred in good faith.

Moreover, correction of the error in the structure of formulae [I] and [II]:

(3) would not introduce any new matter; and

(4) would not require re-examination.

In the Certificate of Correction filed herewith, only the correction of the structure of formulae [I] and [II] to that which was originally filed is sought. Since the specification as filed contained the correct structure, correction of the structure of formulae [I] and [II] would clearly not introduce any new matter. Further, since it is clear from the prosecution history that the error in the structure of formulae [I] and [II] simply went unnoticed during the prosecution and that both the Applicant and the Examiner both thought that the allowed claims contained the correct structure, the requested correction would just as clearly not require re-examination.

For these reasons, it is respectfully requested that the Certificate of Correction filed herewith be granted and issued.

Since all errors are the fault of the Patentee, a credit card payment form for $100.00 is being submitted herewith. 35 U.S.C. § 255 and 37 C.F.R. § 1.323. The requested corrections are attached on Form PTO 1050.

Respectfully submitted,

OBLON, SPIVAK, McCLELLAND,
MAIER & NEUSTADT, P.C.

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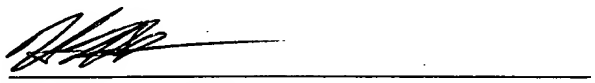


Stephen G. Baxter
Attorney of Record
Registration No. 32,884

Vincent K. Shier, Ph. D.
Registration Number 50,552

UNITED STATES PATENT AND TRADEMARK OFFICE

CERTIFICATE OF CORRECTION

PATENT NO. : 6,170,458

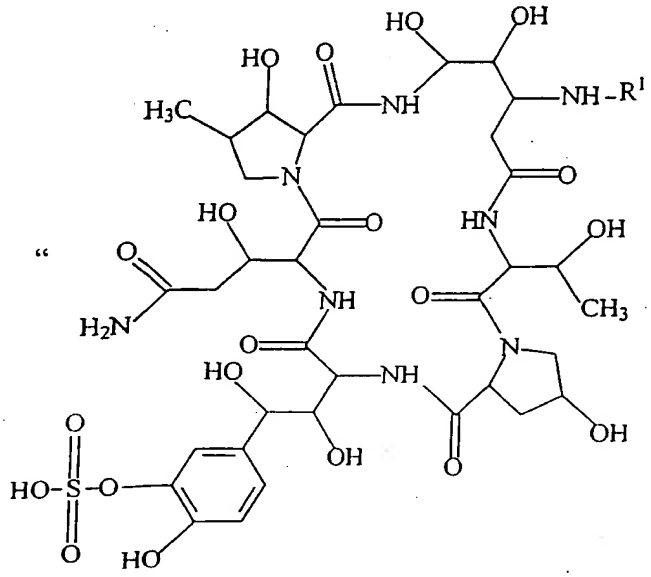
DATED: August 22, 2000

INVENTOR(S): Hidenori OHKI et al.

It is certified that an error appears in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

Column 137, lines 34-54, Claim 1, formula (I):

"

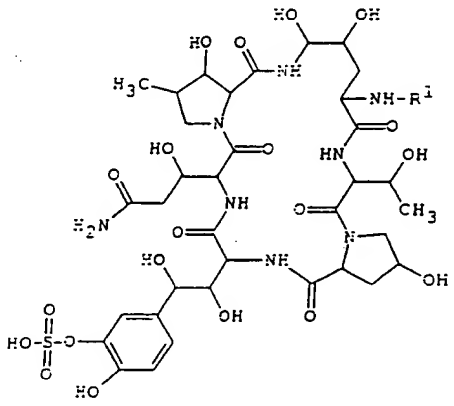


[I]

"

should read:

--



[I]

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UNITED STATES PATENT AND TRADEMARK OFFICE

CERTIFICATE OF CORRECTION

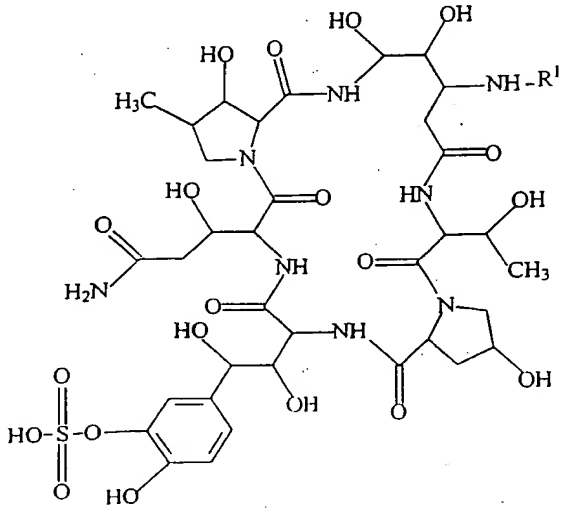
PATENT NO. : 6,170,458

DATED: August 22, 2000

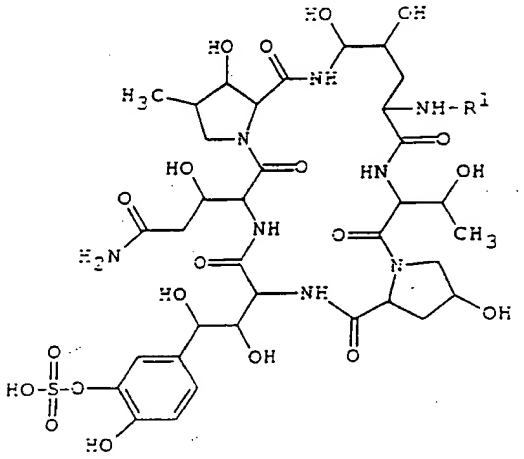
INVENTOR(S): Hidenori OHKI et al.

It is certified that an error appears in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

Column 138, lines 1-23, Claim 3, formula (I):

"  [I] "

should read

--  [I] --

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DATED: August 22, 2000

INVENTOR(S): Hidenori OHKI et al.

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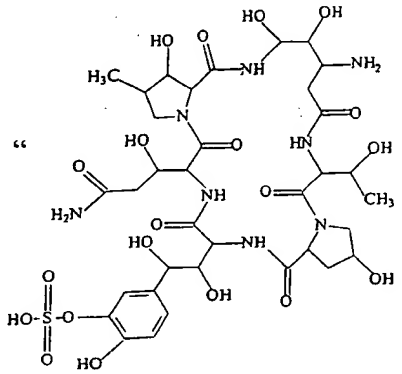
Column 138, lines 28-49, Claim 3, formula (II):

"



(II)

"

should read:

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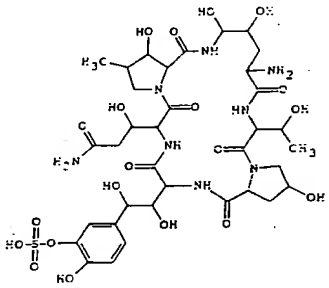

[II]

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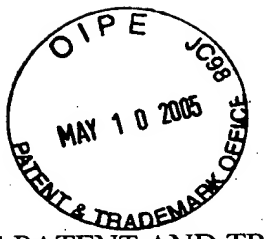

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

IN RE PATENT OF: :
Hidenori OHKI et al :

PATENT NO.: 6,107,458 :

ISSUED: August 22, 2000 :

FOR: CYCLIC HEXAPEPTIDES HAVING ANTIBIOTIC ACTIVITY

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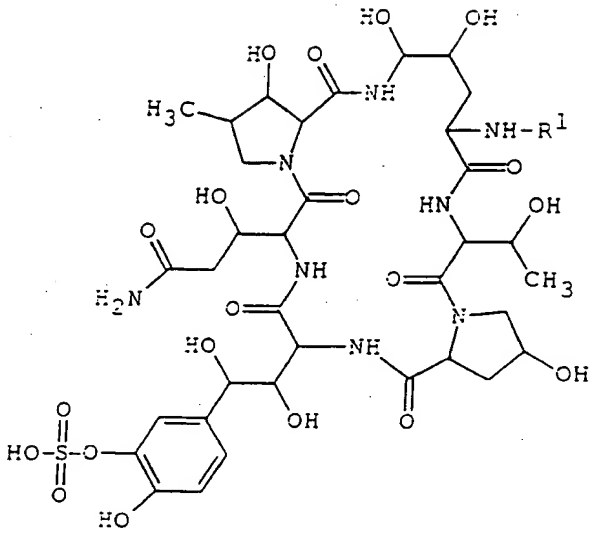

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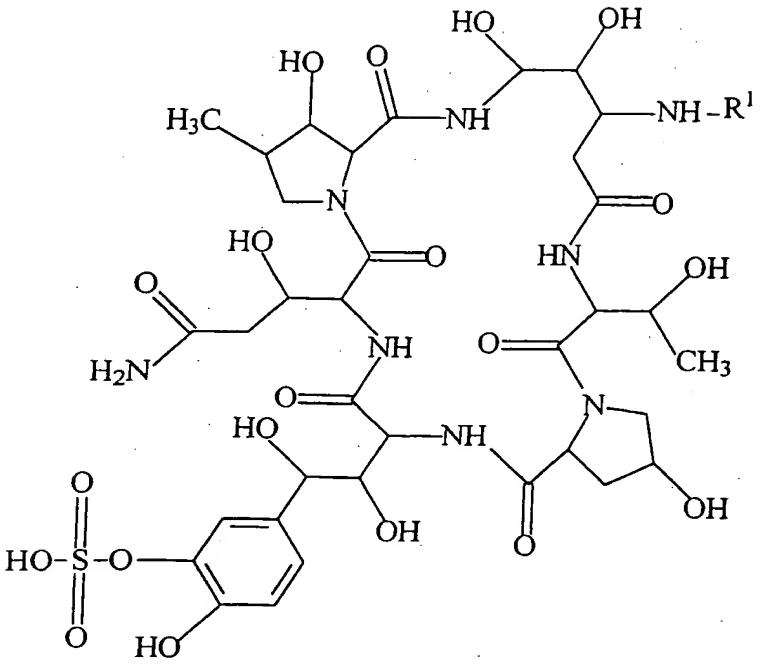

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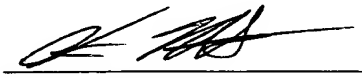

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UNITED STATES PATENT AND TRADEMARK OFFICE

CERTIFICATE OF CORRECTION

PATENT NO. : 6,170,458

DATED: August 22, 2000

INVENTOR(S): Hidenori OHKI et al.

It is certified that an error appears in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

Column 137, lines 34-54, Claim 1, formula (I):

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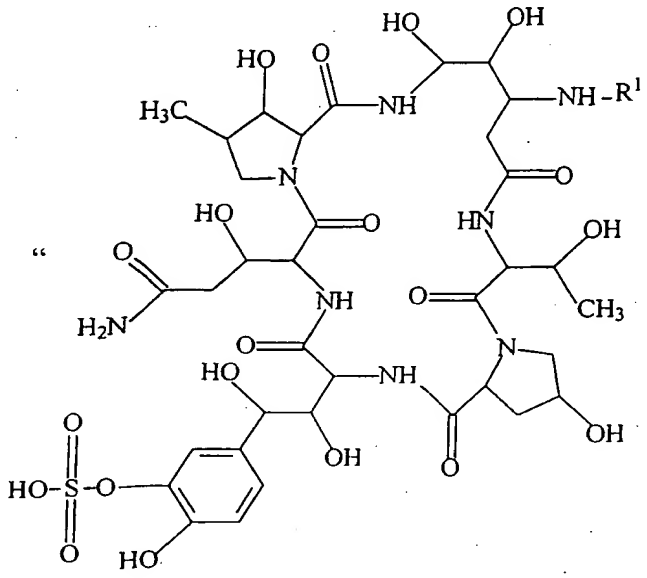

" [I]

should read:

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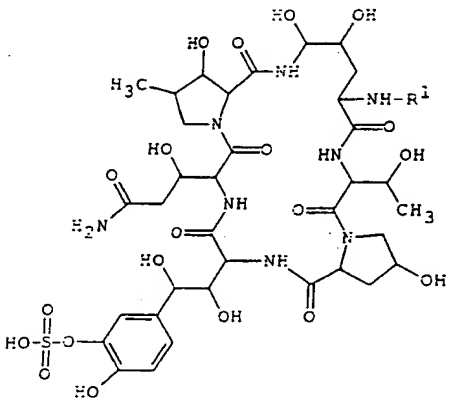

[I] --

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UNITED STATES PATENT AND TRADEMARK OFFICE

CERTIFICATE OF CORRECTION

PATENT NO. : 6,170,458

DATED: August 22, 2000

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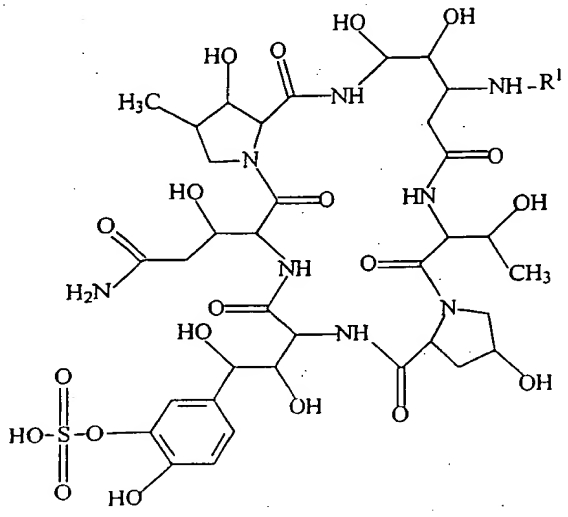
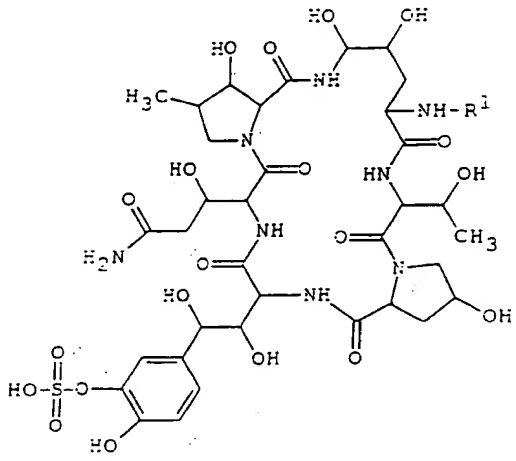
Column 138, lines 1-23, Claim 3, formula (I):

"  [I] "

should read

--  [I] --

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CERTIFICATE OF CORRECTION

PATENT NO. : 6,170,458

DATED: August 22, 2000

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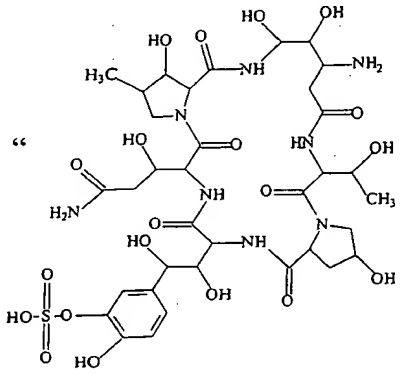
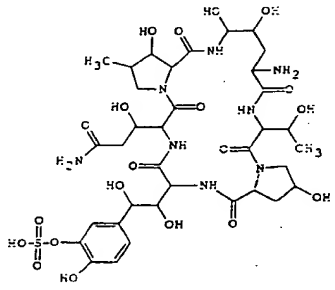
Column 138, lines 28-49, Claim 3, formula (II):

"  (II) "

should read:

--  [II] --

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22850

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(OSMMN 03/02)

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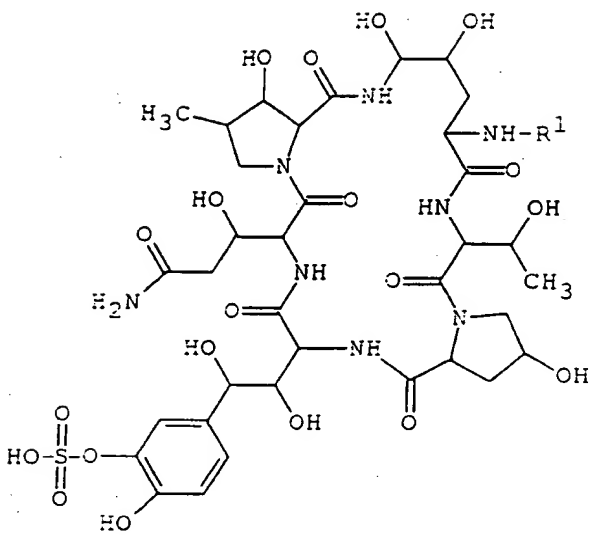
MAY 19 2005

CLAIMS

1. A polypeptide compound of the following general formula :



[I]

wherein R^1 is lower alkanoyl substituted with unsaturated 6-membered heteromonocyclic group containing at least one nitrogen atom which may have one or more suitable substituent(s);

lower alkanoyl substituted with 1,2,3,4-tetrahydroisoquinoline which may have one or more suitable substituent(s);

lower alkanoyl substituted with unsaturated condensed heterocyclic group containing at least one oxygen atom which may have one or more suitable substituent(s);

lower alkanoyl substituted with unsaturated condensed heterocyclic group containing 1 to 3 sulfur atom(s)

which may have one or more suitable substituent(s);

lower alkanoyl substituted with unsaturated condensed heterocyclic group containing 2 or more nitrogen atom(s) which may have one or more suitable substituent(s);

lower alkanoyl substituted with saturated 3 to 8 membered heteromonocyclic group containing at least one nitrogen atom which may have one or more suitable substituent(s);

ar(lower)alkenoyl substituted with aryl which may have one or more suitable substituent(s);

naphthyl(lower)alkenoyl which may have one or more higher alkoxy;

lower alkynoyl which may have one or more suitable substituent(s);

(C_2-C_6)alkanoyl substituted with naphthyl having higher alkoxy;

ar(C_2-C_6)alkanoyl substituted with aryl having one or more suitable substituent(s), in which ar(C_2-C_6)-alkanoyl may have one or more suitable substituent(s);

aroyl substituted with heterocyclic group which may have one or more suitable substituent(s), in which aroyl may have one or more suitable substituent(s);

aroyl substituted with aryl having heterocyclic(higher)alkoxy, in which heterocyclic group may have one or more suitable substituent(s);

aroyl substituted with aryl having lower alkoxy(higher)alkoxy;

aroyl substituted with aryl having lower alkenyl(lower)alkoxy;

aroyl substituted with 2 lower alkoxy;

aroyl substituted with aryl having lower alkyl;

aroyl substituted with aryl having higher alkyl;

aryloxy(lower)alkanoyl which may have one or more suitable substituent(s);

ar(lower)alkoxy(lower)alkanoyl which may have one or more suitable substituent(s);

arylamino(lower)alkanoyl which may have one or more suitable substituent(s);

lower alkanoyl substituted with pyrazolyl which has lower alkyl and aryl having higher alkoxy;

lower alkoxy(higher)alkanoyl, in which higher alkanoyl may have one or more suitable substituent(s);

aroyl substituted with aryl having heterocyclicoxy, in which heterocyclicoxy may have one or more suitable substituent(s);

aroyl substituted with cyclo(lower)alkyl having lower alkyl;

indolylcarbonyl having higher alkyl;

naphthoyl having lower alkyl;

naphthoyl having higher alkyl;

naphthoyl having lower alkoxy(higher)alkoxy;

aroyl substituted with aryl having lower alkoxy(lower)alkoxy(higher)-alkoxy;

aroyl substituted with aryl having lower alkoxy(lower)alkoxy;

aroyl substituted with aryl which has aryl having lower alkoxy;

aroyl substituted with aryl which has aryl having lower alkoxy(lower)alkoxy;

aroyl substituted with aryl having heterocyclicoxy(higher)alkoxy;

aroyl substituted with aryl having aryloxy(lower)alkoxy;

aroyl substituted with aryl having heterocycliccarbonyl(higher)alkoxy;

lower alkanoyl substituted with oxazolyl which has aryl having higher alkoxy;

lower alkanoyl substituted with furyl which has aryl substituted with aryl having lower alkoxy;

lower alkanoyl substituted with triazolyl which has oxo and aryl having higher alkyl;

higher alkanoyl having hydroxy;

higher alkanoyl having ar(lower)alkyl and hydroxy;

3-methyl-tridecenoyl; or

(C_2-C_6)alkanoyl substituted with aryl having higher alkoxy, in which (C_2-C_6)-alkanoyl may have amino or protected amino, and

a pharmaceutically acceptable salt thereof.

2. A compound of claim 1, wherein

R^1 is lower alkanoyl substituted with unsaturated 6-membered heteromonocyclic group containing at least one nitrogen atom which may have 1 to 3 substituent(s) selected from the group consisting of lower alkoxy, higher alkoxy, lower alkyl, higher alkyl, higher alkoxy(lower)alkyl, phenyl having lower alkoxy, phenyl having higher alkoxy, naphthyl having lower alkoxy, naphthyl having higher alkoxy, phenyl having lower alkyl, phenyl having higher alkyl, naphthoyl having higher alkoxy, phenyl substituted with phenyl having lower alkyl, 3 to 8-membered saturated heteromonocyclic group containing at least one nitrogen atom which may have phenyl having higher alkoxy, phenyl substituted with phenyl having lower alkoxy, 3 to 8-membered saturated heteromonocyclic group containing at least one nitrogen atom which may have phenyl having lower alkoxy(higher)alkoxy, 3 to 8-membered saturated heteromonocyclic group containing at least one nitrogen atom which may have phenyl having lower alkoxy, and oxo;

lower alkanoyl substituted with 1,2,3,4-tetrahydroisoquinoline having higher alkoxy and lower alkoxy carbonyl;

lower alkanoyl substituted with unsaturated condensed heterocyclic group containing at least one oxygen atom which may have 1 to 3 substituent(s) selected from the group consisting of lower alkoxy, higher alkoxy, lower alkyl, higher alkyl, higher alkoxy(lower)alkyl, phenyl having lower alkoxy, phenyl having higher alkoxy,

naphthyl having lower alkoxy, naphthyl having higher alkoxy, phenyl having lower alkyl, phenyl having higher alkyl, naphthoyl having higher alkoxy, phenyl substituted with phenyl having lower alkyl, unsaturated 6-membered heteromonocyclic group containing at least one nitrogen atom which may have higher alkoxy, and oxo;

lower alkanoyl substituted with unsaturated condensed heterocyclic group containing 1 to 3 sulfur atom(s) which may have 1 to 3 substituent(s) selected from the group consisting of lower alkoxy, higher alkoxy, lower alkyl, higher alkyl, higher alkoxy(lower)alkyl, phenyl having lower alkoxy, phenyl having higher alkoxy, naphthyl having lower alkoxy, naphthyl having higher alkoxy, phenyl having lower alkyl, phenyl having higher alkyl, naphthoyl having higher alkoxy, phenyl substituted with phenyl having lower alkyl, and oxo;

lower alkanoyl substituted with unsaturated condensed heterocyclic group containing 2 or more nitrogen atoms which may have 1 to 3 substituent(s) selected from the group containing of lower alkoxy, higher alkoxy, lower alkyl, higher alkyl, higher alkoxy(lower)alkyl, phenyl having lower alkoxy, phenyl having higher alkoxy, naphthyl having lower alkoxy, naphthyl having higher alkoxy, phenyl having lower alkyl, phenyl having higher alkyl, naphthoyl having higher alkoxy, phenyl substituted with phenyl having lower alkyl, and oxo; or

lower alkanoyl substituted with saturated 3 to 8-membered heteromonocyclic group containing at least one nitrogen atom which may have 1 to 3

substituent(s) selected from the group consisting of lower alkoxy, higher alkoxy, lower alkyl, higher alkyl, higher alkoxy(lower)alkyl, phenyl having lower alkoxy, phenyl having higher alkoxy, naphthyl having lower alkoxy, naphthyl having higher alkoxy, phenyl having lower alkyl, phenyl having higher alkyl, naphthoyl having higher alkoxy, phenyl substituted with phenyl having lower alkyl, and oxo.

3. A compound of claim 1, wherein

R^1 is ar(lower)alkenoyl substituted with aryl which may have 1 to 3 substituent(s) selected from the group consisting of lower alkoxy, higher alkoxy, lower alkyl, higher alkyl, higher alkoxy(lower)alkyl, phenyl having lower alkoxy, phenyl having higher alkoxy, naphthyl having lower alkoxy, naphthyl having higher alkoxy, phenyl having lower alkyl, phenyl having higher alkyl, naphthoyl having higher alkoxy, phenyl substituted with phenyl having lower alkyl, lower alkoxy(lower)alkyl, halo(lower)alkoxy, lower alkenyloxy, halo(higher)alkoxy, lower alkoxy(higher)alkoxy, and oxo;

naphthyl(lower)alkenoyl which may have 1 to 3 higher alkoxy;

lower alkynoyl which may have 1 to 3 substituent(s) selected from the group consisting of lower alkoxy, higher alkoxy, lower alkyl, higher alkyl, higher alkoxy(lower)alkyl, phenyl having lower alkoxy, phenyl having higher alkoxy, naphthyl having lower alkoxy, naphthyl having higher alkoxy, phenyl having lower alkyl, phenyl having higher alkyl, naphthoyl having higher alkoxy, phenyl substituted with phenyl having

lower alkyl, and oxo;

ar(C_2-C_6)alkanoyl substituted with aryl having 1 to 3 substituent(s) selected from the group consisting of lower alkoxy, higher alkoxy, lower alkyl, higher alkyl, higher alkoxy(lower)alkyl, phenyl having lower alkoxy, phenyl having higher alkoxy, naphthyl having lower alkoxy, naphthyl having higher alkoxy, phenyl having lower alkyl, phenyl having higher alkyl, naphthoyl having higher alkoxy, phenyl substituted with phenyl having lower alkyl, phenyl having lower alkoxy(lower)alkoxy, and oxo, in which ar(C_2-C_6)-alkanoyl may have hydroxy, oxo, protected amino or amino; or

(C_2-C_6)alkanoyl substituted with naphthyl having higher alkoxy.

4. A compound of claim 1, wherein

R^1 is aroyl substituted with heterocyclic group which may have 1 to 3 substituent(s) selected from the group consisting of lower alkoxy, higher alkoxy, lower alkyl, higher alkyl, higher alkoxy(lower)alkyl, phenyl having lower alkoxy, phenyl having higher alkoxy, naphthyl having lower alkoxy, naphthyl having higher alkoxy, phenyl having lower alkyl, phenyl having higher alkyl, naphthoyl having higher alkoxy, phenyl substituted with phenyl having lower alkyl, phenyl having lower alkoxy(higher)alkoxy, phenyl having higher alkenyloxy, heterocyclic group substituted with phenyl having lower alkoxy, heterocyclic group, cyclo(lower)alkyl having phenyl, phenyl having cyclo(lower)alkyl, phenyl substituted with heterocyclic group having lower alkyl and oxo, cyclo(lower)alkyl having lower alkyl, phenyl

substituted with phenyl having lower alkoxy, phenyl having heterocyclic group and oxo, in which aroyl may have halogen;

aroyl substituted with aryl having heterocyclic(higher)alkoxy, in which heterocyclic group may have lower alkyl;

aroyl substituted with aryl having lower alkoxy(higher)alkoxy;

aroyl substituted with aryl having lower alkenyl(lower)alkoxy;

aroyl substituted with 2 lower alkoxy;

aroyl substituted with aryl having lower alkyl; or

aroyl substituted with aryl having higher alkyl.

5. A compound of claim 1, wherein

R^1 is aryloxy(lower)alkanoyl which may have 1 to 3 substituent(s) selected from the group consisting of lower alkoxy, higher alkoxy, lower alkyl, higher alkyl, higher alkoxy(lower)alkyl, phenyl having lower alkoxy, phenyl having higher alkoxy, naphthyl having lower alkoxy, naphthyl having higher alkoxy, phenyl having lower alkyl, phenyl having higher alkyl, naphthoyl having higher alkoxy, phenyl substituted with phenyl having lower alkyl, and oxo;

ar(lower)alkoxy(lower)alkanoyl which may have 1 to 3 substituent(s) selected from the group consisting of lower alkoxy, higher alkoxy, lower alkyl, higher alkyl, higher alkoxy(lower)alkyl, phenyl having lower alkoxy, phenyl having higher alkoxy, naphthyl having lower alkoxy, naphthyl having higher alkoxy, phenyl having lower alkyl, phenyl having higher alkyl, naphthoyl having higher alkoxy, phenyl substituted with phenyl

having lower alkyl, and oxo; or

arylamino(lower)alkanoyl which may have 1 to 3 substituent(s) selected from the group consisting of lower alkoxy, higher alkoxy, lower alkyl, higher alkyl, higher alkoxy(lower)alkyl, phenyl having lower alkoxy, phenyl having higher alkoxy, naphthyl having lower alkoxy, naphthyl having higher alkoxy, phenyl having lower alkyl, phenyl having higher alkyl, naphthoyl having higher alkoxy, phenyl substituted with phenyl having lower alkyl, and oxo.

6. A compound of claim 1, wherein

R^1 is lower alkanoyl substituted with pyrazolyl which has lower alkyl and aryl having higher alkoxy;

lower alkoxy(higher)alkanoyl, in which higher alkanoyl may have amino or protected amino;

aroyl substituted with aryl having heterocyclicoxy, in which heterocyclicoxy may have phenyl;

aroyl substituted with cyclo(lower)alkyl having lower alkyl;

indolylcarbonyl having higher alkyl;

naphthoyl having lower alkyl;

naphthoyl having higher alkyl;

naphthoyl having lower alkoxy(higher)alkoxy;

aroyl substituted with aryl having lower alkoxy(lower)alkoxy(higher)alkoxy;

aroyl substituted with aryl having lower alkoxy(lower)alkoxy;

aroyl substituted with aryl which has phenyl having lower alkoxy;

aroyl substituted with aryl which has phenyl having lower alkoxy(lower)alkoxy;

aroyl substituted with aryl having

heterocyclicoxy(higher)alkoxy;

aroyl substituted with aryl having phenoxy(lower)alkoxy;

aroyl substituted with aryl having heterocycliccarbonyl(higher)alkoxy;

lower alkanoyl substituted with oxazolyl which has aryl having higher alkoxy;

lower alkanoyl substituted with furyl which has aryl substituted with phenyl having lower alkoxy;

lower alkanoyl substituted with triazolyl which has oxo and phenyl having higher alkyl;

higher alkanoyl having hydroxy;

higher alkanoyl having benzyl and hydroxy;

3-methyl-tridecenoyl; or

(C_2-C_6)alkanoyl substituted with aryl having higher alkoxy, in which (C_2-C_6)alkanoyl may have amino or protected amino.

7. A compound of claim 2, wherein

R^1 is lower alkanoyl substituted with pyridyl or pyridazinyl, each of which may have 1 to 3 substituent(s) selected from the group consisting of higher alkoxy, higher alkoxy(lower)alkyl, phenyl having higher alkoxy, phenyl substituted with phenyl having lower alkoxy, piperazinyl substituted with phenyl having higher alkoxy, piperazinyl substituted with phenyl having lower alkoxy(higher)alkoxy, and piperazinyl substituted with phenyl having lower alkoxy;

lower alkanoyl substituted with 1,2,3,4-tetrahydroisoquinoline having higher alkoxy and lower alkoxy carbonyl;

lower alkanoyl substituted with coumarin which may have 1 to 3 substituent(s) selected from the group consisting of higher alkoxy, and oxo;

lower alkanoyl substituted with benzothiophenyl which may have 1 to 3 higher alkoxy;

lower alkanoyl substituted with benzo[b]furanyl which may have 1 to 3 substituent(s) selected from the group consisting of higher alkoxy and lower alkyl;

lower alkanoyl substituted with benzooxazolyl which may have 1 to 3 substituent(s) selected from the group consisting of higher alkyl, phenyl having lower alkoxy, phenyl substituted with phenyl having lower alkyl, and pyridyl having higher alkoxy;

lower alkanoyl substituted with benzimidazolyl which may have 1 to 3 substituent(s) selected from the group consisting of higher alkyl, and phenyl having lower alkoxy; or

lower alkanoyl substituted with piperidyl or piperazinyl, each of which may have 1 to 3 substituent(s) selected from the group consisting of phenyl having higher alkoxy, and naphthoyl having higher alkoxy.

8. A compound of claim 3, wherein

R^1 is phenyl(lower)alkenoyl substituted with phenyl which may have 1 to 3 substituent(s) selected from the group consisting of lower alkoxy, lower alkyl, higher alkyl, lower alkoxy(lower)alkyl, halo(lower)alkoxy, lower alkenyloxy, halo(higher)alkoxy, and lower alkoxy(higher)alkoxy;

naphthyl(lower)alkenoyl which may have 1 to 3 higher alkoxy;

lower alkynoyl which may have 1 to 3 substituent(s) selected from the group consisting of naphthyl having higher alkoxy, and phenyl

substituted with phenyl having lower alkyl;

phenyl(C_2-C_6)alkanoyl substituted with phenyl which has 1 to 3 substituent(s) selected from the group consisting of lower alkoxy, higher alkoxy, lower alkyl, higher alkyl, and phenyl having lower alkoxy(lower)alkyl,

in which phenyl(C_2-C_6)alkanoyl may have hydroxy, oxo, protected amino or amino; or

(C_2-C_6)alkanoyl substituted with naphthyl having higher alkoxy.

9. A compound of claim 4, wherein

R^1 is benzoyl substituted with saturated 6-membered heteromonocyclic group containing at least one nitrogen atom which may have 1 to 3 substituent(s) selected from the group consisting of phenyl having lower alkoxy, phenyl having higher alkoxy, phenyl having lower alkyl, phenyl having lower alkoxy(higher)alkoxy, phenyl having higher alkenyloxy, piperidyl substituted with phenyl having lower alkoxy, piperidyl, cyclo(lower)alkyl having phenyl, phenyl having cyclo(lower)alkyl, and phenyl substituted with triazolyl having oxo and lower alkyl,

in which benzoyl may have halogen;

benzoyl substituted with unsaturated 5-membered heteromonocyclic group containing 1 to 2 oxygen atom(s) and 1 to 3 nitrogen atom(s) which may have 1 to 3 substituent(s) selected from the group consisting of higher alkyl, phenyl having lower alkoxy, phenyl having higher alkoxy, phenyl having lower alkoxy(higher)alkoxy, and phenyl substituted with phenyl having lower alkoxy;

benzoyl substituted with 5 or 6-membered heteromonoccyclic group containing 1 or 2 nitrogen

atom(s) which may have 1 to 3 substituent(s) selected from the group consisting of higher alkyl and phenyl having lower alkoxy;

benzoyl substituted with 5-membered heteromonocyclic group containing 1 to 2 nitrogen atom(s) and 1 to 2 sulfur atom(s) which may have 1 to 3 substituent(s) selected from the group consisting of phenyl having lower alkoxy, phenyl having higher alkoxy, cyclo(lower)alkyl having lower alkyl, phenyl substituted with phenyl having lower alkoxy, phenyl having cyclo(lower)alkyl, phenyl having piperidine, and phenyl having lower alkoxy(higher)alkoxy;

benzoyl substituted with phenyl having higher alkoxy substituted with unsaturated 3 to 8-membered heteromonocyclic group containing at least one nitrogen atom;

benzoyl substituted with phenyl having higher alkoxy substituted with saturated 6-membered heteromonocyclic group containing 1 to 2 oxygen atom(s) and 1 to 3 nitrogen atom(s) which may have lower alkyl;

benzoyl substituted with phenyl having lower alkoxy(higher)alkoxy;

benzoyl substituted with phenyl having lower alkenyl(lower)alkoxy;

benzoyl substituted with 2 lower alkoxy;

benzoyl substituted with phenyl having lower alkyl; or

benzoyl substituted with phenyl having higher alkyl.

10. A compound of claim 5, wherein

R^1 is phenyloxy(lower)alkanoyl which may have 1 to 3 higher alkoxy;

phenyl(lower)alkoxy(lower)alkanoyl which may have 1 to 3 higher alkoxy; or

phenylamino(lower)alkanoyl which may have 1 to 3 higher alkoxy.

11. A compound of claim 1, wherein

R^1 is benzoyl substituted with piperazinyl which may have 1 to 3 substituent(s) selected from the group consisting of phenyl having lower alkoxy, phenyl having higher alkoxy, phenyl having lower alkyl, phenyl having lower alkoxy(higher)alkoxy, phenyl having higher alkenyloxy, piperidyl substituted with phenyl having lower alkoxy, cyclo(lower)alkyl having phenyl, phenyl having cyclo(lower)alkyl, and phenyl substituted with triazolyl having oxo and lower alkyl,

in which benzoyl may have halogen;

benzoyl substituted with isoxazolyl which may have 1 to 3 substituent(s) selected from the group consisting of higher alkyl, phenyl having lower alkoxy, phenyl having higher alkoxy, phenyl having lower alkoxy(higher)alkoxy, and phenyl substituted with phenyl having lower alkoxy;

benzoyl substituted with phenyl having lower alkoxy(higher)alkoxy;

benzoyl substituted with phenyl having lower alkyl;

benzoyl substituted with phenyl having higher alkyl;

phenyl(lower)alkenoyl substituted with phenyl which may have 1 to 3 substituent(s) selected from the group consisting of lower alkoxy, lower alkyl, higher alkyl, lower alkoxy(lower)alkyl, halo(lower)alkoxy, lower alkenyloxy, halo(higher)alkoxy and lower alkoxy(higher)alkoxy;

benzoyl substituted with thiadiazolyl which may have 1 to 3 substituent(s) selected from the group consisting of phenyl having lower alkoxy, phenyl having higher alkoxy, cyclo(lower)alkyl having lower alkyl, phenyl substituted with phenyl having lower alkoxy, phenyl having cyclo(lower)alkyl, phenyl having piperidyl, and phenyl having lower alkoxy(higher)alkoxy; or

benzoyl substituted with oxadiazolyl which may have 1 to 3 substituent(s) selected from the group consisting of phenyl having lower alkoxy, phenyl having higher alkoxy, phenyl having lower alkoxy(higher)alkoxy, higher alkyl and phenyl substituted with phenyl having lower alkoxy.

12. A compound of claim 11, wherein

R^1 is benzoyl substituted with phenyl having lower alkoxy(higher)alkoxy; or

benzoyl substituted with phenyl having lower alkyl.

13. A compound of claim 11, wherein

R^1 is benzoyl substituted with piperazinyl which may have phenyl having lower alkoxy;

benzoyl substituted with isoxazolyl which may have phenyl having lower alkoxy;

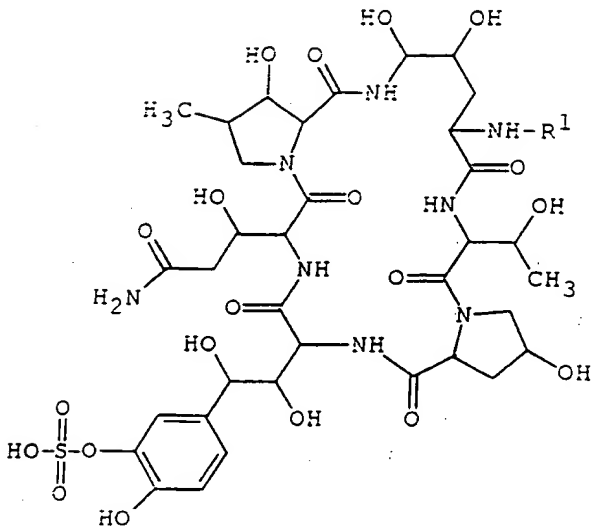
benzoyl substituted with thiadiazolyl which may have phenyl having lower alkoxy(higher)alkoxy; or

benzoyl substituted with oxadiazolyl which may have phenyl having lower alkoxy.

14. A compound of claim 11, wherein

R^1 is phenyl(lower)alkenoyl substituted with phenyl which may have lower alkoxy.

15. A process for the preparation of a polypeptide compound of the formula [I] :



[I]

wherein

R^1 is lower alkanoyl substituted with unsaturated 6-membered heteromonocyclic group containing at least one nitrogen atom which may have one or more suitable substituent(s);

lower alkanoyl substituted with 1,2,3,4-tetrahydro-isoquinoline having higher alkoxy;

lower alkanoyl substituted with unsaturated condensed heterocyclic group containing at least one oxygen atom which may have one or more suitable substituent(s);

lower alkanoyl substituted with unsaturated condensed heterocyclic group containing 1 to 3 sulfur atom(s) which may have one or more suitable substituent(s);

lower alkanoyl substituted with unsaturated condensed heterocyclic group containing 2 or more nitrogen atom(s) which may have one or more suitable substituent(s);

lower alkanoyl substituted with saturated 3 to 8-membered heteromonocyclic group containing at least one nitrogen atom which may have one or more suitable substituent(s);

ar(lower)alkenoyl substituted with aryl which may have one or more suitable substituent(s);

naphthyl(lower)alkenoyl which may have one or more higher alkoxy;

lower alkynoyl which may have one or more suitable substituent(s);

(C_2-C_6)alkanoyl substituted with naphthyl having higher alkoxy;

ar(C_2-C_6)alkanoyl substituted with aryl having one or more suitable substituent(s), in which ar(C_2-C_6)alkanoyl may have one or more suitable substituent(s);

aroyl substituted with heterocyclic group which may have one or more suitable substituent(s), in which aroyl may have one or more suitable substituent(s);

aroyl substituted with aryl having heterocyclic(higher)alkoxy, in which heterocyclic group may have one or more suitable substituent(s);

aroyl substituted with aryl having lower alkoxy(higher)alkoxy;

aroyl substituted with aryl having lower alkenyl(lower)alkoxy;

aroyl substituted with 2 lower alkoxy;

aroyl substituted with aryl having lower alkyl;

aroyl substituted with aryl having higher alkyl;

aryloxy(lower)alkanoyl which may have one or more suitable substituent(s);

ar(lower)alkoxy(lower)alkanoyl which may have one or more suitable substituent(s);

arylamino(lower)alkanoyl which may have one or more suitable substituent(s);

lower alkanoyl substituted with pyrazolyl which has lower alkyl and aryl having higher alkoxy;

lower alkoxy(higher)alkanoyl, in which higher alkanoyl may have one or more suitable substituent(s);

aroyl substituted with aryl having heterocyclicoxy, in which heterocyclicoxy may have one or more suitable substituent(s);

aroyl substituted with cyclo(lower)alkyl having lower alkyl;

indolylcarbonyl having higher alkyl;

naphthoyl having lower alkyl;

naphthoyl having higher alkyl;

naphthoyl having lower alkoxy(higher)alkoxy;

aroyl substituted with aryl having lower alkoxy(lower)alkoxy(higher)alkoxy;

aroyl substituted with aryl having lower alkoxy(lower)alkoxy;

aroyl substituted with aryl which has aryl having lower alkoxy;

aroyl substituted with aryl which has aryl having lower alkoxy(lower)alkoxy;

aroyl substituted with aryl having heterocyclicoxy(higher)alkoxy;

aroyl substituted with aryl having aryloxy(lower)alkoxy;

aroyl substituted with aryl having heterocycliccarbonyl(higher)alkoxy;

lower alkanoyl substituted with oxazolyl which has aryl having higher alkoxy;

lower alkanoyl substituted with furyl which has aryl substituted with aryl having lower alkoxy;

lower alkanoyl substituted with triazolyl which

has oxo and aryl having higher alkyl;

higher alkanoyl having hydroxy;

higher alkanoyl having ar(lower)alkyl and hydroxy;

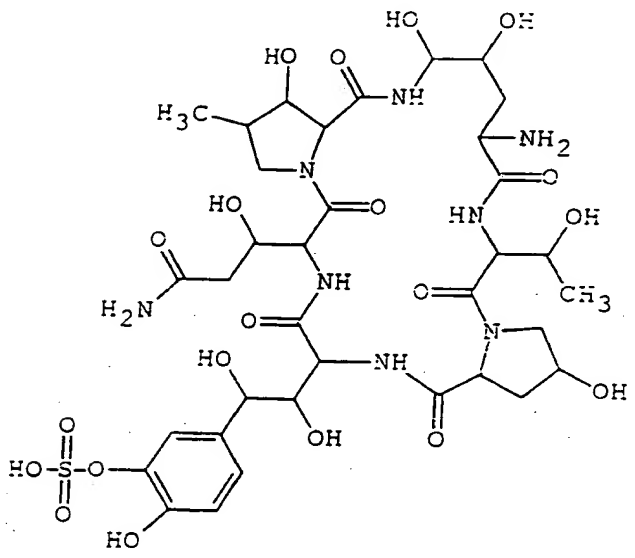
3-methyl-tridecenoyl; or

(C_2-C_6)alkanoyl substituted with aryl having higher alkoxy, in which (C_2-C_6)alkanoyl may have amino or protected amino, and

a pharmaceutically acceptable salt thereof,

which comprises

1) reacting a compound of the formula :



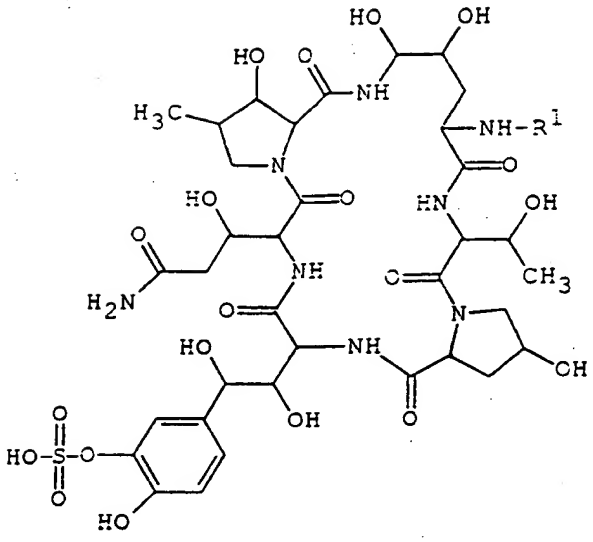
[II]

or its reactive derivative at the amino group or a salt thereof, with a compound of the formula :

$$R^1 - OH \qquad [III]$$

wherein R^1 is defined above,

or its reactive derivative at the carboxy group or a salt thereof, to give a compound [I] of the formula :



[I]

wherein R^1 is defined above,

or a salt thereof.

16. A pharmaceutical composition which comprises, as an active ingredient, a compound of claim 1 or a pharmaceutically acceptable salt thereof in admixture with pharmaceutically acceptable carriers or excipients.

17. Use of a compound of claim 1 or a pharmaceutically acceptable salt thereof as a medicament.

18. A compound of claim 1 or a pharmaceutically acceptable salt thereof for use as a medicament.

19. A method for the prophylactic and/or the therapeutic treatment of infectious diseases caused by pathogenic microorganisms which comprises administering a compound of claim 1 or a pharmaceutically acceptable salt thereof to a human being or an animal.

THN
8-29-97

UNITED STATES DEPARTMENT OF COMMERCE
Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

SERIAL NUMBER	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
08/809,723	05/21/97	OHKI H	18-971-0-PCT

EXAMINER

18M1/0828

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1755 JEFFERSON DAVIS HIGHWAY
ARLINGTON VA 22202

ART UNIT	PAPER NUMBER
1811	5

DATE MAILED: 08/28/97

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

RD 11-28-97

☑ This application has been examined ☐ Responsive to communication filed on _____ ☐ This action is made final.

A shortened statutory period for response to this action is set to expire 3 month(s), 0 days from the date of this letter.
Failure to respond within the period for response will cause the application to become abandoned. 35 U.S.C. 133

Part I THE FOLLOWING ATTACHMENT(S) ARE PART OF THIS ACTION:

1. ☑ Notice of References Cited by Examiner, PTO-892.
2. ☐ Notice of Draftsman's Patent Drawing Review, PTO-948.
3. ☐ Notice of Art Cited by Applicant, PTO-1449.
4. ☐ Notice of Informal Patent Application, PTO-152.
5. ☐ Information on How to Effect Drawing Changes, PTO-1474.
6. ☐ _____

Part II SUMMARY OF ACTION

1. ☑ Claims 1-19 are pending in the application.
   Of the above, claims _____ are withdrawn from consideration.
2. ☐ Claims _____ have been cancelled.
3. ☐ Claims _____ are allowed.
4. ☑ Claims 1-19 are rejected.
5. ☐ Claims _____ are objected to.
6. ☐ Claims _____ are subject to restriction or election requirement.
7. ☐ This application has been filed with informal drawings under 37 C.F.R. 1.85 which are acceptable for examination purposes.
8. ☐ Formal drawings are required in response to this Office action.
9. ☐ The corrected or substitute drawings have been received on _____. Under 37 C.F.R. 1.84 these drawings are ☐ acceptable; ☐ not acceptable (see explanation or Notice of Draftsman's Patent Drawing Review, PTO-948).
10. ☐ The proposed additional or substitute sheet(s) of drawings, filed on _____, has (have) been ☐ approved by the examiner; ☐ disapproved by the examiner (see explanation).
11. ☐ The proposed drawing correction, filed _____, has been ☐ approved; ☐ disapproved (see explanation).
12. ☐ Acknowledgement is made of the claim for priority under 35 U.S.C. 119. The certified copy has ☐ been received ☐ not been received ☐ been filed in parent application, serial no. _____; filed on _____.
13. ☐ Since this application apppears to be in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under Ex parte Quayle, 1935 C.D. 11; 453 O.G. 213.
14. ☐ Other

1. Claims 17-18 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 17 provides for the use of a compound or a salt thereof as a medicament, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

Claim 17 is rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd v. Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966)

Claim 18 is a duplicate of claim 1 because claim 18 has no further structural limitation that would distinguish the compounds recited in claim 18 from those recited in claim 1.

Claim Rejections - 35 USC § 103

2. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Toshiro et al (EPA 0462531) or Toshrio et al (USP 5,376634).

The present invention relates to compounds that have the generally formula set forth on pages 2-5 of the specification. The instant compounds have antimicrobial activity. Additionally, the invention also relates to a process of making said compounds.

Toshiro et al (EPA 0462531) teaches antimicrobial compounds which read on the compound of the present invention, especially when R1 is acyl, R2 is hydroxyl, and R3 is hydrosulfonyloxy, and R4 is carbamoyl provided that R1 is not palimitoyl . The compounds of the present invention fall with the scope of the invention taught by Toshiro et al. Therefore it would be obvious to one of ordinary skill in the art to preferentially selective the appropriate radicals needed to prepare the compounds of the present invention. Furthermore it would be within the skill of the art and therefore obvious to use the process taught by Toshiro et al to prepare the peptides of the instant invention, wherein the compounds have antimicrobial activity.

The non-statutory double patenting rejection, whether of the obviousness-type or non-obviousness-type, is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent. *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); and *In re Goodman*, 29 USPQ2d 2010 (Fed. Cir. 1993).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(b) and © may be used to overcome an actual or provisional rejection based on a non-statutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.78(d).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-19 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims of U.S. Patent No. 5,374634. Although the conflicting claims are not identical, they are not patentably distinct from each other because the invention are co-extensive. Essentially, the present invention relates to compounds, pharmaceutical compositions, and a methods of making compounds set forth on pages 2-5 of the specification. The compounds of the instant invention fall within the scope of the invention taught by Toshiro et al; therefore it is within the skill of the art to preferentially select the appropriate radicals for preparing the compounds of the invention, wherein the compounds have antimicrobial activity.

The lengthy specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However,

this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth on the attached Notice To Comply With Requirements For Patent Applicants Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures.

3. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sandra Marshall whose telephone number is (703) 308-1030.

Sgm
August 26, 1997

CECILIA J. TSANG
SUPERVISORY PATENT EXAMINER
GROUP 1800

NOTICE TO COMPLY WITH REQUIREMENTS FOR PATENT APPLICATIONS CONTAINING NUCLEOTIDE SEQUENCE AND/OR AMINO ACID SEQUENCE DISCLOSURES

The nucleotide and/or amino acid sequence disclosure contained in this application do not comply with the requirements for such a disclosure as set forth in 37 CFR 1.821 - 1.825 for the following reason(s):

☑ 1. This application clearly fails to comply with the requirements of 37 CFR 1.821 - 1.825. Applicant's attention is directed to these regulations, published at 1114 O.G. May 15, 1990 and at 55 FR 18230, May 1, 1990.

☑ 2. This application does not contain, as a separate part of the disclosure on paper copy, a "Sequence Listing" as required by 37 CFR 1.821(c).

☑ 3. A copy of the "Sequence Listing" in computer readable form has not been submitted as required by 37 CFR 1.821(e).

☐ 4. A copy of the "Sequence Listing" in computer readable form has been submitted. However, the content of the computer readable form does not comply with the requirements of 37 CFR 1.822 and/or 1.823, as indicated on the attached copy of the marked-up "Raw Sequence Listing."

☐ 5. The computer readable form that has been filed with this application has been found to be damaged and/or unreadable as indicated on the attached CRF Diskette Problem Report. A substitute computer readable form must be submitted as required by 37 CFR 1.825(d).

☐ 6. The paper copy of the "Sequence Listing" is not the same as the computer readable form of the "Sequence Listing" as required by 37 CFR 1.821(e).

☐ 7.

Other: _____

Applicant must provide:

☑ An initial or substitute computer readable form (CRF) copy of the "Sequence Listing"

☑ An initial or substitute paper copy of the "Sequence Listing", as well as an amendment directing its entry into the specification

☑ A statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 CFR 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d)

For questions regarding compliance with these requirements, please contact:

For Rules Interpretation, call (703) 308-1123
For CRF submission help, call (703) 308-4212
For PatentIn software help, call (703) 557-0400

Please return a copy of this notice with your response.

TO SEPARATE, HOLD TOP AND BOTTOM EDGES, SNAP APART AND DISCARD CARBON

FORM PTO-892 (REV. 2-92) U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE

NOTICE OF REFERENCES CITED

SERIAL NO.	GROUP ART UNIT	ATTACHMENT TO PAPER NUMBER
08/809723	1811	20

APPLICANT(S): OHKI ET AL

MAY 10 2005 PATENT & TRADEMARK OFFICE

U.S. PATENT DOCUMENTS

*		DOCUMENT NO.	DATE	NAME	CLASS	SUB-CLASS	FILING DATE IF APPROPRIATE
	A	5376634	12/27/94	Iwamoto et al	530	317	
	B						
	C						
	D						
	E						
	F						
	G						
	H						
	I						
	J						
	K						

FOREIGN PATENT DOCUMENTS

*		DOCUMENT NO.	DATE	COUNTRY	NAME	CLASS	SUB-CLASS	PERTINENT SHTS. DWG	PERTINENT PP. SPEC.
*	L	0462531	12/27/91	EP					
	M								
	N								
	O								
	P								
	Q								

OTHER REFERENCES (Including Author, Title, Date, Pertinent Pages, Etc.)

R	
S	
T	
U	

EXAMINER	DATE
SANDRA MARSHALL	8-26-05

* A copy of this reference is not being furnished with this office action.
(See Manual of Patent Examining Procedure, section 707.05 (a).)

THN
6-8-98

UNITED STATES DEPARTMENT OF COMMERCE
Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
08/809,723	05/21/97	Ged.1	18-971-0PCT

08/809.723

18-971-0PCT

HM11/0605

OBLON SPIVAK MCCLELLAND
MAIER AND NEUSTADT
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1755 JEFFERSON DAVIS HIGHWAY
ARLINGTON VA 22202

EXAMINER
MARSHALL, S

ART UNIT	PAPER NUMBER
1654	

DATE MAILED: 06/05/98

RD 9-5-98
NA 10-5-98 (1st)

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
08/809723	Ohki et al
Examiner	**Group Art Unit**
Marshall	1654

—The MAILING DATE of this communication appears on the cover sheet beneath the correspondence address—

Period for Response

A SHORTENED STATUTORY PERIOD FOR RESPONSE IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a response be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for response specified above is less than thirty (30) days, a response within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for response is specified above, such period shall, by default, expire SIX (6) MONTHS from the mailing date of this communication .
- Failure to respond within the set or extended period for response will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

Status

☐ Responsive to communication(s) filed on _____.

☒ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 1 1; 453 O.G. 213.

Disposition of Claims

☒ Claim(s) 1-16 and 19 is/are pending in the application.

Of the above claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) 1-16 and 19 is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claim(s) _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119 (a)-(d)

☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 11 9(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 1 7.2(a)).

*Certified copies not received: _____.

Attachment(s)

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of References Cited, PTO-892

☐ Notice of Informal Patent Application, PTO-152

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Other _____

Office Action Summary

Claims 1-16 and 19 are pending in the case, and claims 17-18 have been cancel.

The rejection of claims 1-16 and 19 under 103(a) as being unpatentable over Toshiro et al (EPA0462531) or Toshiro et al (Us Patent 5, 376634) has been maintained as set forth in the office action mailed August 28, 1997 on pages 2-3 . Additionally, the rejection of claims 1-16 and 19 under the judicially created doctrine of obviousness-typed double patenting has been maintained.

Applicant's arguments filed March 2, 1998 have been fully considered but they are not persuasive.

Applicants agree with the examiner that the compounds of instant invention falls within the scope of the invention as taught by Toshiro et al. However, applicants' argue that the examiner provides no reason as to why one of skill in the art would be motivated from the teaching of the reference, to pick the specific acyl group of the instant invention.

Although the patent of Toshiro et al teaches R1 is acyl, Toshiro et al also define acyl groups as being lower alkanoyl, e.g. formyl , acetyl , propionyl, butyl... which may be substituted....(see Toshiro et al, col. 6, lines 30-68), , of which the preferred acyl is lower alkanoyl, including heterocyclic lower alkanoyl (see col.8, lines 14-68). These compounds read essentially on the compounds of applicants(see spec. 2-20) Therefore the compounds of the instant invention largely overlap the compounds of the reference, and one of ordinary skill in the art at the time that the invention was made would have been motivated to preferentially select the desired acyl group to obtain compounds of the instant invention that possess anitmicrobial

activity, especially anti fungal activity. Applicants' situation is not an In re Baird situation. In in re Baird, one would have to pick and choose from various radicals to come up with the claimed invention. In this invention, (their) is a large overlap in the compounds.

The Declaration submitted by applicants has been carefully considered, however; the small number of peptides tested is not commensurate in scope with the protection sought.Therefore the rejections are maintained. However, the specific compounds tested and showed unexpected results are allowable if presented.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

1. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sandra Marshall whose telephone number is (703) 308-1030.

sgm
June 4, 1998

C Tsang

CECILIA J. TSANG
SUPERVISORY PATENT EXAMINER
GROUP 1800

DOCKET NO: 18-971-0 PCT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

IN RE APPLICATION OF:	:	
HIDENORI OHKI, ET AL.	:	GROUP ART UNIT: 1654
SERIAL NO: 08/809,723	:	EXAMINER: MARSHALL, S.
FILED: MAY 21, 1997	:	

FOR: CYCLIC HEXAPEPTIDES HAVING ANTIBIOTIC ACTIVITY

AMENDMENT PURSUANT TO 37 C.F.R.§1.116

ASSISTANT COMMISSIONER FOR PATENTS
WASHINGTON, D.C. 20231

SIR:

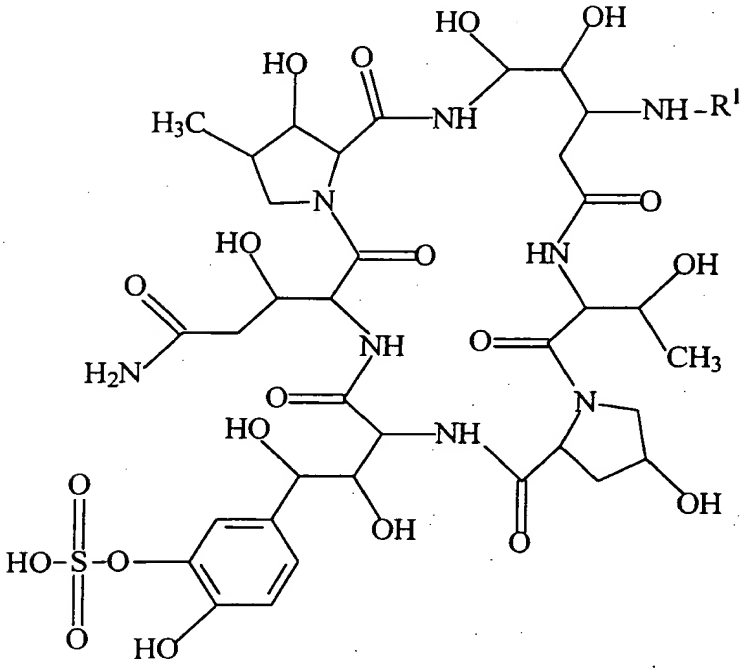
Responsive to the outstanding Office Action issued June 5, 1998, entry of the following amendments and remarks is respectfully requested. The amendment does not raise any new issues and serves to place the application in better form for appeal by reducing or simplifying the issues.

IN THE CLAIMS:

Please cancel Claims 1-16 and 19.

Please add the following new Claims:

--20. A polypeptide compound of the following general formula [I]:



[I]

wherein R^1 is selected from the group consisting of:

naphthyl (lower) alkenoyl which may have one or more higher alkoxy;

(C_2-C_6) alkanoyl substituted with naphthyl having higher alkoxy;

ar (C_2-C_6) alkanoyl substituted with aryl having one or more suitable substituent(s), wherein ar (C_2-C_6)-alkanoyl may have one or more suitable substituent(s);

aroyl substituted with a heterocyclic group which may have one or more suitable substituent(s), wherein aroyl may have one or more suitable substituent(s); and

a pharmaceutically acceptable salt thereof.

21. A compound of Claim 20, wherein R^1 is selected from the group consisting of:

naphthyl (lower) alkenoyl which may have 1 to 3 higher alkoxy;

ar (C_2-C_6) alkanoyl substituted with aryl having 1 to 3 substituent(s) selected from the

group consisting of lower alkoxy, higher alkoxy, lower alkyl, higher alkyl, higher alkoxy (lower) alkyl, phenyl having lower alkoxy, phenyl having higher alkoxy, naphthyl having lower alkoxy, naphthyl having higher alkoxy, phenyl having lower alkyl, phenyl having higher alkyl, naphthoyl having higher alkoxy, phenyl substituted with phenyl having lower alkyl, phenyl having lower alkoxy (lower) alkoxy, and oxo, wherein ar (C_2-C_6)-alkanoyl may have hydroxy, oxo, protected amino or amino; and

(C_2-C_6) alkanoyl substituted with naphthyl having higher alkoxy.

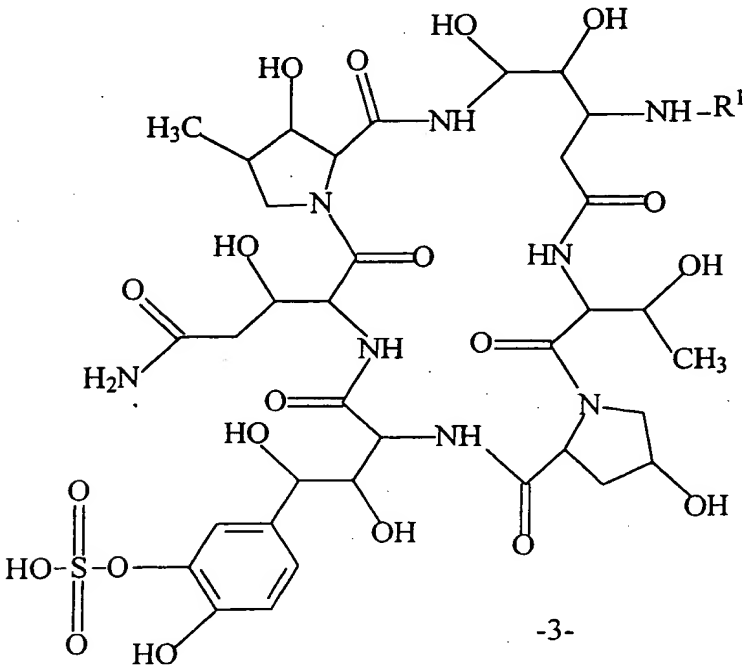
22. A compound of Claim 21, wherein R^1 is selected from the group consisting of:

naphthyl (lower) alkenoyl which may have 1 to 3 higher alkoxy;

phenyl (C_2-C_6) alkanoyl substituted with phenyl which has 1 to 3 substituent(s) selected from the group consisting of lower alkoxy, higher alkoxy, lower alkyl, higher alkyl, and phenyl having lower alkoxy (lower) alkyl, wherein phenyl (C_2-C_6) alkanoyl may have hydroxy, oxo, protected amino or amino; and

(C_2-C_6) alkanoyl substituted with naphthyl having higher alkoxy.

23. A polypeptide having the following general formula [I]:



[I]

wherein R^1 is aroyl substituted with a heterocyclic group which may have one or more suitable substituent(s), wherein aroyl may have one or more suitable substituent(s).

24. A compound of Claim 23, wherein R^1 is aroyl substituted with a heterocyclic group which may have 1 to 3 substituent(s) selected from the group consisting of lower alkoxy, higher alkoxy, lower alkyl, higher alkyl, higher alkoxy (lower) alkyl, phenyl having lower alkoxy, phenyl having higher alkoxy, naphthyl having lower alkoxy, naphthyl having higher alkoxy, phenyl having lower alkyl, phenyl having higher alkyl, naphthoyl having higher alkoxy, phenyl substituted with phenyl having lower alkyl, phenyl having lower alkoxy (higher) alkoxy, phenyl having higher alkenyloxy, a heterocyclic group substituted with phenyl having lower alkoxy, a heterocyclic group, cyclo (lower) alkyl having phenyl, phenyl having cyclo (lower) alkyl, phenyl substituted with a heterocyclic group having lower alkyl and oxo, cyclo (lower) alkyl having lower alkyl, phenyl substituted with phenyl having lower alkoxy, and phenyl having a heterocyclic group and oxo, and wherein aroyl may also be substituted with halogen.

25. A compound of Claim 24, wherein R^1 is selected from the group consisting of:

benzoyl substituted with a saturated 6-membered heteromonocyclic group containing at least one nitrogen atom which may have 1 to 3 substituent(s) selected from the group consisting of phenyl having lower alkoxy, phenyl having higher alkoxy, phenyl having lower alkyl, phenyl having lower alkoxy (higher) alkoxy, phenyl having higher alkenyloxy, piperidyl substituted with phenyl having lower alkoxy, piperidyl, cyclo (lower) alkyl having phenyl, phenyl having cyclo (lower) alkyl, and phenyl substituted with triazolyl having oxo and lower alkyl, wherein benzoyl may also be substituted with halogen;

benzoyl substituted with an unsaturated 5-membered heteromonocyclic group

containing 1 to 2 oxygen atom(s) and 1 to 3 nitrogen atom(s) which may have 1 to 3 substituent(s) selected from the group consisting of higher alkyl, phenyl having lower alkoxy, phenyl having higher alkoxy, phenyl having lower alkoxy (higher) alkoxy, and phenyl substituted with phenyl having lower alkoxy;

benzoyl substituted with a 5 or 6-membered heteromonocyclic group containing 1 or 2 nitrogen atom(s) which may have 1 to 3 substituent(s) selected from the group consisting of higher alkyl and phenyl having lower alkoxy; and

benzoyl substituted with a 5-membered heteromonocyclic group containing 1 to 2 nitrogen atom(s) and 1 to 2 sulfur atom(s) which may have 1 to 3 substituent(s) selected from the group consisting of phenyl having lower alkoxy, phenyl having higher alkoxy, cyclo (lower) alkyl having lower alkyl, phenyl substituted with phenyl having lower alkoxy, phenyl having cyclo (lower) alkyl, phenyl having piperidine, and phenyl having lower alkoxy (higher) alkoxy.

26. The compound of Claim 23, wherein R^1 is selected from the group consisting of:

benzoyl substituted with piperazinyl which may have 1 to 3 substituent(s) selected from the group consisting of phenyl having lower alkoxy, phenyl having higher alkoxy, phenyl having lower alkyl, phenyl having lower alkoxy (higher) alkoxy, phenyl having higher alkenyloxy, piperidyl substituted with phenyl having lower alkoxy, cyclo (lower) alkyl having phenyl, phenyl having cyclo (lower) alkyl, and phenyl substituted with triazolyl having oxo and lower alkyl, and wherein benzoyl may also be substituted with halogen;

benzoyl substituted with isoxazolyl which may have 1 to 3 substituent(s) selected from the group consisting of higher alkyl, phenyl having lower alkoxy, phenyl having higher alkoxy, phenyl having lower alkoxy (higher) alkoxy, and phenyl substituted with phenyl

having lower alkoxy;

benzoyl substituted with thiadiazolyl which may have 1 to 3 substituent(s) selected from the group consisting of phenyl having lower alkoxy, phenyl having higher alkoxy, cyclo (lower) alkyl having lower alkyl, phenyl substituted with phenyl having lower alkoxy, phenyl having cyclo (lower) alkyl, phenyl having piperidyl, and phenyl having lower alkoxy (higher) alkoxy; and

benzoyl substituted with oxadiazolyl which may have 1 to 3 substituent(s) selected from the group consisting of phenyl having lower alkoxy, phenyl having higher alkoxy, phenyl having lower alkoxy (higher) alkoxy, higher alkyl and phenyl substituted with phenyl having lower alkoxy.

27. A compound of Claim 26, wherein R^1 is selected from the group consisting of:

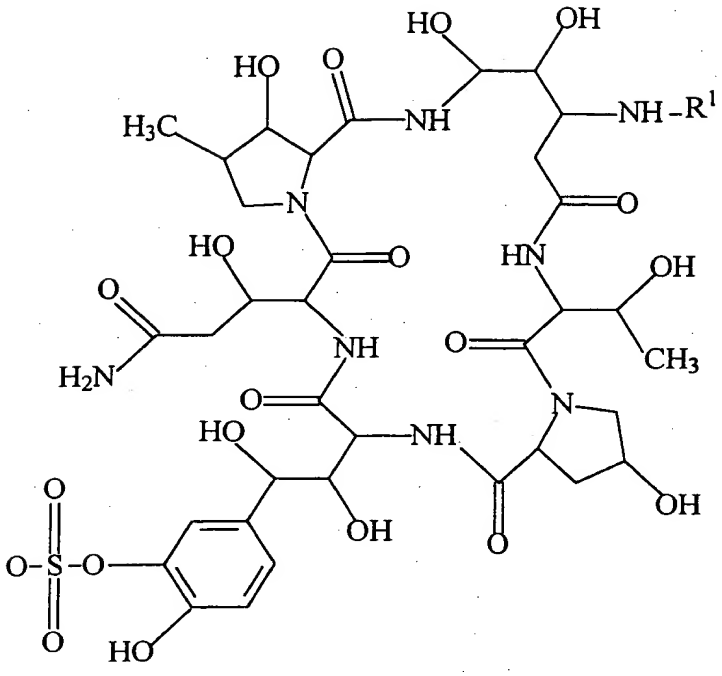
benzoyl substituted with piperazinyl which may have phenyl having lower alkoxy;

benzoyl substituted with isoxazolyl which may have phenyl having lower alkoxy;

benzoyl substituted with thiadiazolyl which may have phenyl having lower alkoxy (higher) alkoxy; and

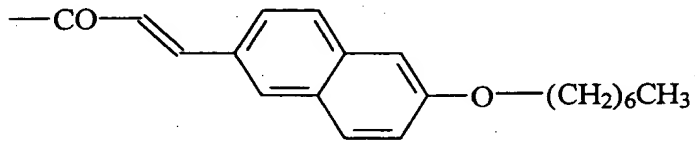
benzoyl substituted with oxadiazolyl which may have phenyl having lower alkoxy.

28. A polypeptide compound of the following general formula [I]:



[I]

wherein R^1 is selected from the group consisting of:



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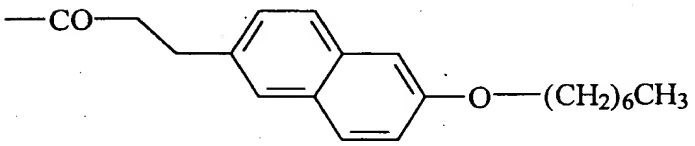

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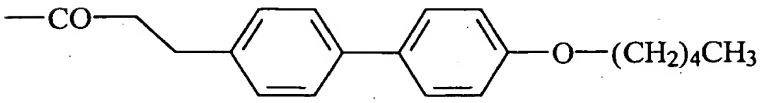

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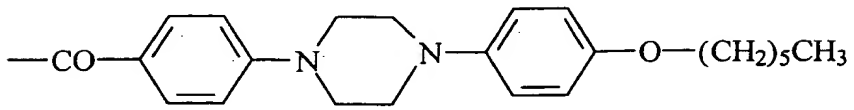
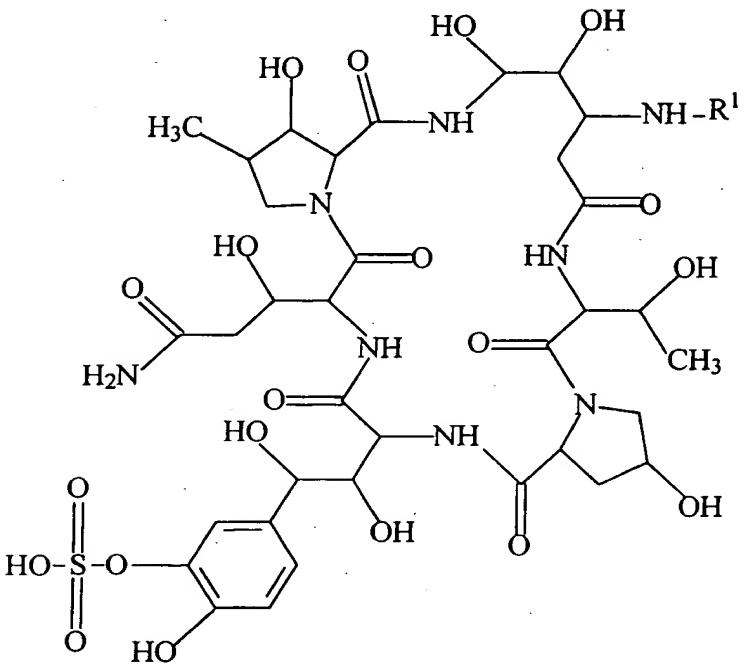


and a pharmaceutically acceptable salt thereof.

29. A process for the preparation of a polypeptide compound of the formula [I]:



[I]

wherein R^1 is selected from the group consisting of:

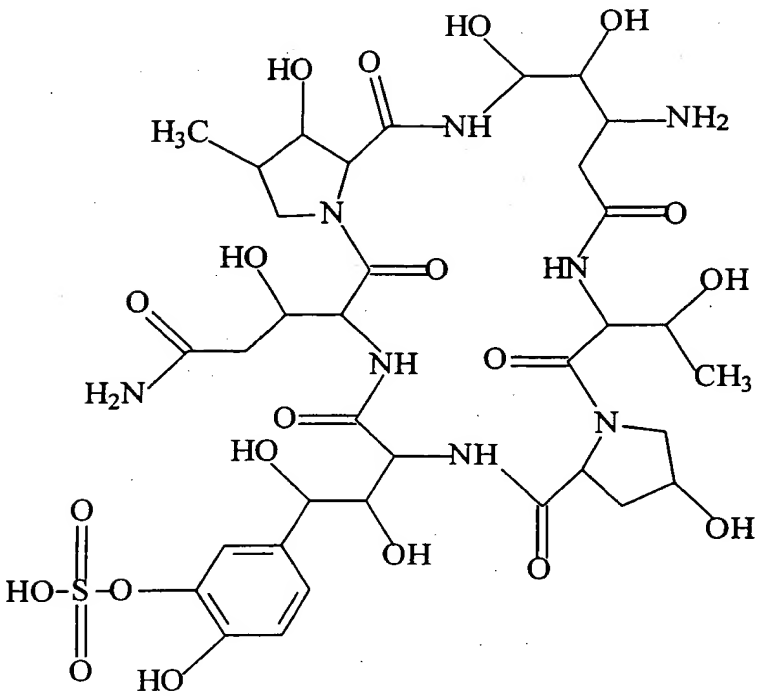
(C_2-C_6) alkanoyl substituted with naphthyl having higher alkoxy;

ar (C_2-C_6) alkanoyl substituted with aryl having one or more suitable substituent(s), wherein ar (C_2-C_6) alkanoyl may have one or more suitable substituent(s);

aroyl substituted with a heterocyclic group which may have one or more suitable substituent(s), in which aroyl may have one or more suitable substituent(s); and a pharmaceutically acceptable salt thereof,

which comprises

1) reacting a compound of the formula [II]:



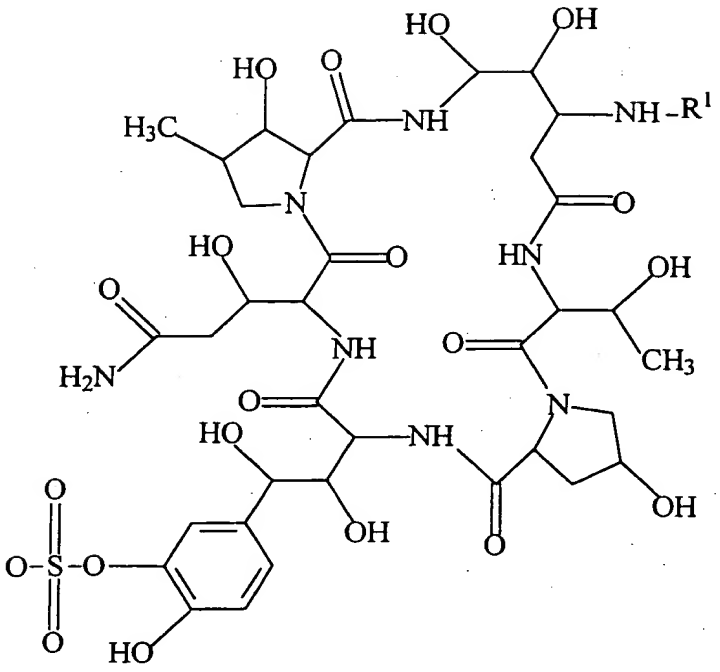
[II]

or its reactive derivative at the amino group or a salt thereof, with a compound of the formula [III]:

$$R^1 - OH \qquad [III]$$

wherein R^1 is defined above,

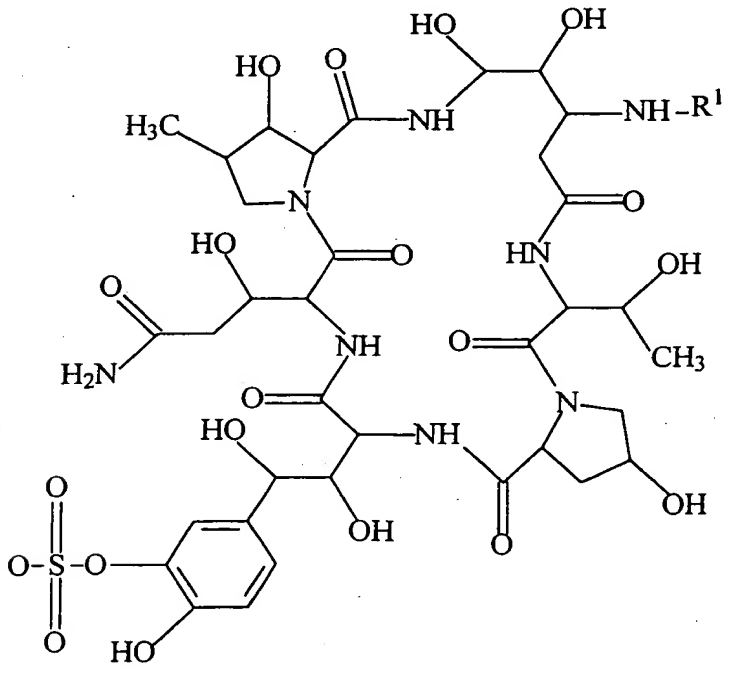
or its reactive derivative at the carboxy group or a salt thereof, to give a compound [I] of the formula:



[I]

wherein R^1 is defined above, or a salt thereof.

30. A process for the preparation of a polypeptide compound of the formula [I]:



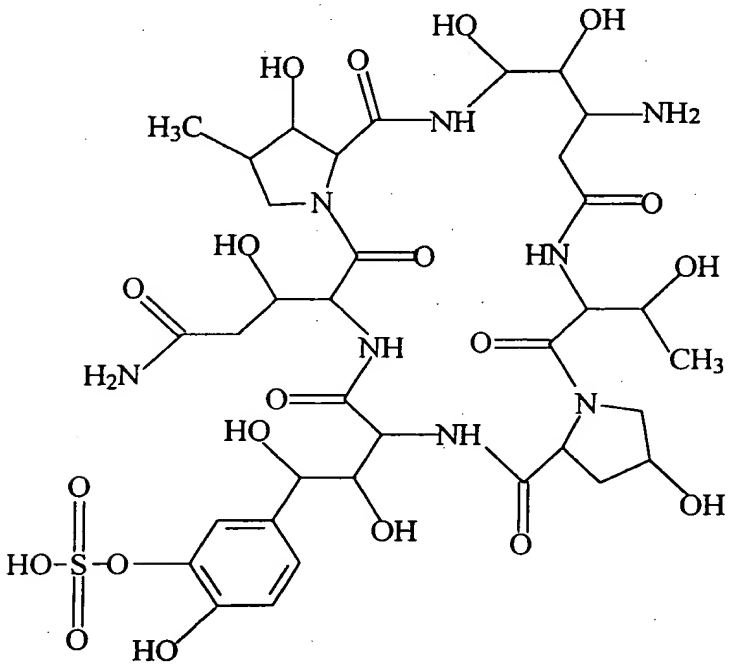
[I]

wherein R^1 is aroyl substituted with a heterocyclic group which may have one or more suitable substituent(s), in which aroyl may have one or more suitable substituent(s) or

a pharmaceutically acceptable salt thereof,

which comprises

1) reacting a compound of the formula [II]:



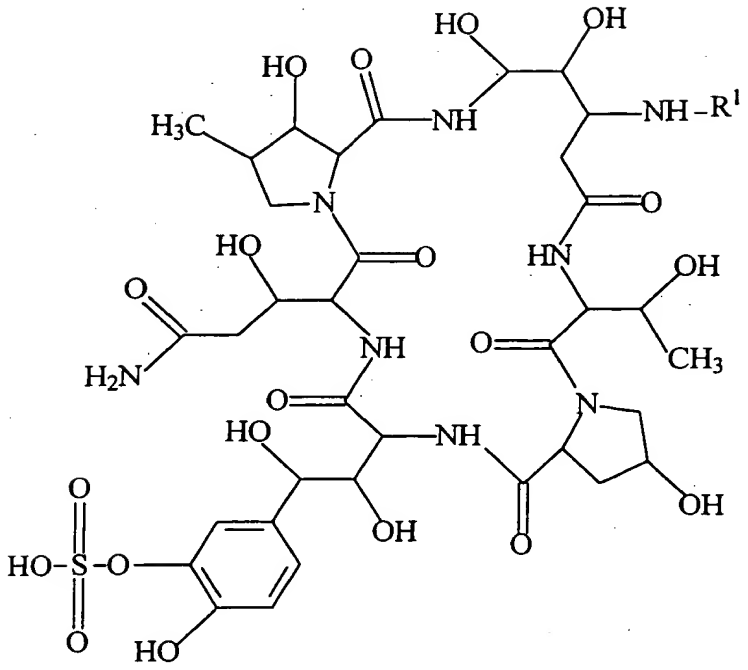
[II]

or its reactive derivative at the amino group or a salt thereof, with a compound of the formula [III]:

$$R^1 - OH \qquad [III]$$

wherein R^1 is defined above,

or its reactive derivative at the carboxy group or a salt thereof, to give a compound [I] of the formula:



[I]

wherein R^1 is defined above, or a salt thereof.

31. A pharmaceutical composition which comprises, as an active ingredient, a compound of Claim 20 or a pharmaceutically acceptable salt thereof in admixture with pharmaceutically acceptable carriers of excipients.

32. A pharmaceutical composition which comprises, as an active ingredient, a compound of Claim 23 or a pharmaceutically acceptable salt thereof in admixture with pharmaceutically acceptable carriers of excipients.

33. A method for the prophylactic and/or the therapeutic treatment of infectious diseases caused by pathogenic microorganisms which comprises administering a compound of Claim 20 or a pharmaceutically acceptable salt thereof to a human being or an animal.

34. A method for the prophylactic and/or the therapeutic treatment of infectious diseases caused by pathogenic microorganisms which comprises administering a compound

of Claim 23 or a pharmaceutically acceptable salt thereof to a human being or an animal.

35. A pharmaceutical composition which comprises, as an active ingredient, a compound of Claim 28 or a pharmaceutically acceptable salt thereof in admixture with pharmaceutically acceptable carriers of excipients.

36. A method for the prophylactic and/or the therapeutic treatment of infectious diseases caused by pathogenic microorganisms which comprises administering a compound of Claim 28 or a pharmaceutically acceptable salt thereof to a human being or an animal.--

SUPPORT FOR THE AMENDMENTS

New Claims 20-36 are supported by original Claims 1-16 and 19. Support for Claim 28 can be found on page 17 of the specification as originally filed. No new matter has been added. Claims 20-36 remain active in the case.

REMARKS

Applicants appreciate the interview granted undersigned counsel in the above-captioned application, wherein it was argued that new Claim 20 is commensurate in scope with the showing of superior results using the claimed compounds, presented in the Declaration under 37 C.F.R. §1.132 filed March 2, 1998, since the compounds encompassed by Claim 20 are homologs of the specific compounds tested. The Examiner agreed to give the arguments presented in a request for reconsideration careful consideration. Applicants appreciate the Examiner's acknowledgment that the specific compounds tested showed unexpected results and would be allowable if presented in independent form.

The present invention relates to cyclic hexapeptide compounds having antimicrobial activity in humans and animals, a process for preparing the compounds, a pharmaceutical

composition containing the compound and a method of using the compounds for the prophylactic or therapeutic treatment of infectious diseases.

The rejection of Claims 1-16 and 19 under 103(a) over Toshiro et al. (EP A 0462531) or Toshiro et al. (US Patent 5,376,634) is respectfully traversed.

Since the disclosure of US 5,376,634 appears to be identical to EP 0 462 531, the following discussion applies to both references.

Toshiro et al. does not disclose Applicant's cyclic hexapeptide. The R_1 substituent on the compounds of Toshiro et al. may be either hydrogen or acyl, whereas in the presently claimed compounds it must be acyl. Toshiro et al. disclose that suitable acyl groups are those listed at column 6, line 30 through column 8, line 5. This encompasses hundreds of compounds. However, none of the acyl groups described is an aroyl substituted with a heterocyclic group, as recited in Claim 23 of the instant application. The only description of R_1 being an aroyl group is at column 7, line 44, but there is no description of the aroyl group being substituted with a heterocyclic group. Nor are there any examples in Toshiro et al. of compounds wherein the R_1 is aroyl substitued with a heterocyclic group. Therefore it is respectfully submitted that independent Claims 23 and 30, wherein R_1 is aroyl substituted with a heterocyclic group and Claims 24-27, 32 and 34, dependent therefrom, are all patentable over Toshiro et al.

Applicants have shown, via the Declaration filed March 2, 1998, the superiority of the presently claimed compounds compared to two of the preferred compounds in Toshiro et al. The Examiner agreed that a claim to those specific compounds would be allowable if presented. Therefore, Applicants have presented Claim 28, which is drawn to examples 16, 20, 21 and 23 from the specification which were shown in the Declaration to have superior

antifungal properties compared to two of the preferred compounds in Toshiro et al. Therefore, Claim 28 and Claims 35 and 36, dependent therefrom are submitted to be patentable over Toshiro et al.

Claim 20 has been limited to four choices for R^1 which are submitted to be representative of the compounds of Examples 16, 20, 21 and 23, shown to have superior antifungal activity. Specifically, R^1 may be: naphthyl(lower)alkenoyl which may have one or more higher alkoxy, which is representative of the compound of Example 21 in which R^1 is naphthyl-C_2-alkenoyl having a C_7-alkoxy group; (C_2-C_6) alkanoyl substituted with naphthyl having higher alkoxy, which is representative of the compound of Example 20 in which R^1 is C_2 alkanoyl substituted with naphthyl having a C_7 alkoxy group; ar(C_2-C_6)alkanoyl substituted with aryl having one or more suitable substituents, which is representative of the compound of Example 16 in which R^1 is phenyl-C_2-alkanoyl substituted with phenyl having C_7 alkoxy; and aroyl substituted with a heterocyclic group which may have one or more suitable substituents, which is representative of the compound of Example 23 in which R^1 is phenoyl substituted with piperazinyl which is substituted with phenyl having a C_6 alkoxy group. The above-described R^1 groups should be considered to be representative of the specific compounds shown in the Declaration since they are homologs, i.e., a family of related compounds, the composition of which varies from member to member by a CH_2 group. Chemists knowing the properties of one member would in general know what to expect in adjacent members. Objective evidence of nonobviousness must be commensurate in scope with the claims which the evidence is offered to support. By the same token, Applicant is not required to test each and every species within the scope of the claims. Rather, patentability is established by a showing of unexpected superiority for <u>representative</u>

compounds within the scope of the claims. Ex parte Winters, 11 USPQ2d 1387 (Bd. Pat. App. & Int. 1988). Applicants submit that the compounds tested are representative of the scope of the compounds recited in Claim 20 since they are homologs. Therefore, it is respectfully requested that the rejection be withdrawn.

The rejection of Claims 1-19 under the judicially created doctrine of obviousness-type double patenting over the claims of U.S. Patent 5,374,634, to Toshiro et al., is respectfully traversed.

This rejection is traversed based on the showing of unexpectedly superior antifungal properties of the claimed compounds. Additionally, this rejection is improper for Claims 23 and 30 and Claims 24-27, 32 and 34, since there is no disclosure or suggestion that R_1 is an aroyl substituted with a heterocyclic group in the specification or the claims of Toshiro et al. Therefore, it is respectfully requested that this rejection be withdrawn.

Applicants submit that the application is now in condition for allowance, and an early notification of such action is earnestly solicited.

Respectfully submitted,

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18-0971-0 PCT

IN THE UNITED STATES PATENT & TRADEMARK OFFICE

IN RE APPLICATION OF :

HIDENORI OHKI ET AL : EXAMINER: MARSHALL

SERIAL NO: 08/809,723 :

FILED: MAY 21, 1997 : GROUP ART UNIT: 1654

FOR: CYCLIC HEXAPEPTIDES : HAVING ANTIBIOTIC ACTIVITY

PRELIMINARY AMENDMENT

ASSISTANT COMMISSIONER FOR PATENTS
WASHINGTON, D.C. 20231

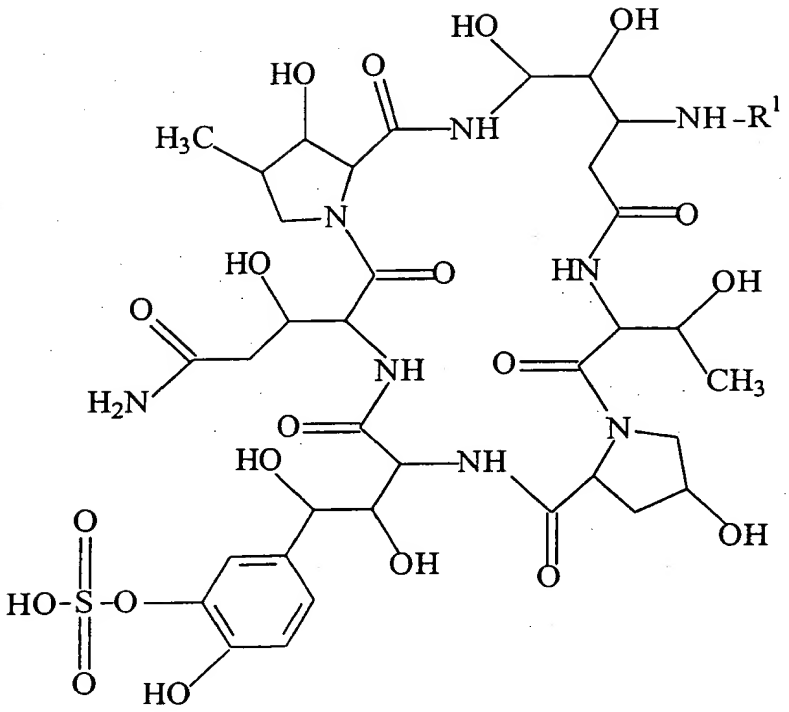
SIR:

Prior to examination please amend the above-identified application as follows:

IN THE CLAIMS

Cancel claims 20-36. Please add the following new claims:

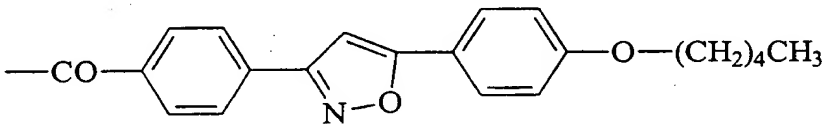
--37. A polypeptide compound of the following general formula (I):



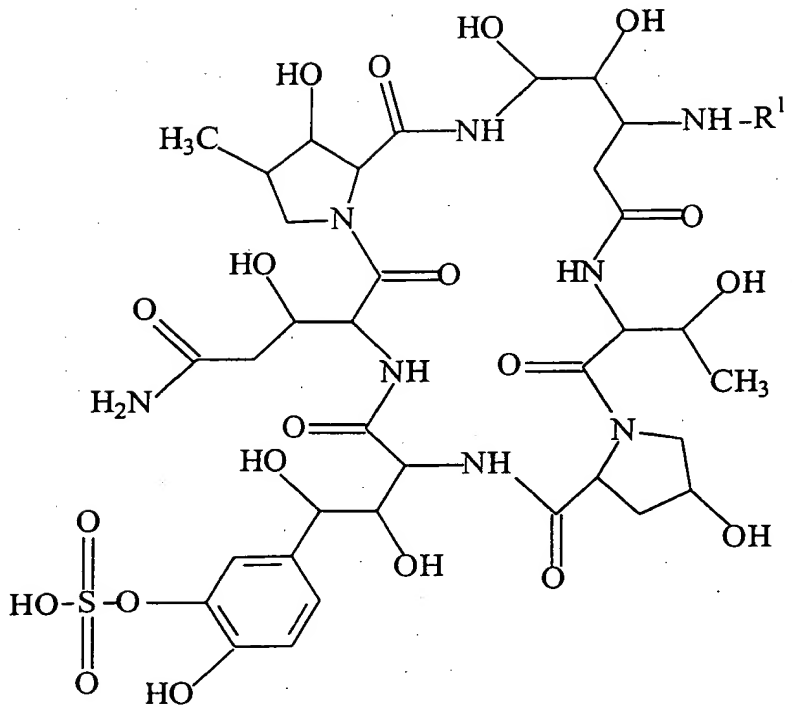
(I)

wherein R^1 is benzoyl substituted with isoxazolyl which has phenyl having lower alkoxy, or a salt thereof.

38. A compound of claim 37, wherein R^1 is



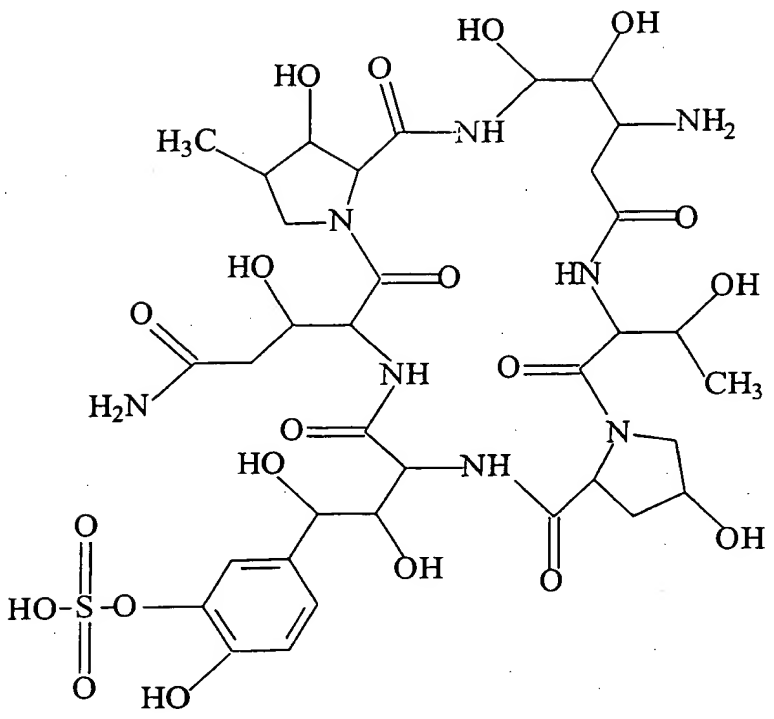
39. A process for the preparation of a polypeptide compound of the formula (I):



(I)

wherein R^1 is benzoyl substituted with isoxazolyl which has phenyl having lower alkoxy, or a salt thereof, said process comprising:

1) reacting a compound of the formula (II):



(II)

or its reactive derivative at the amino group or a salt thereof, with a compound of formula (III):

$$R^1\text{-}OH \qquad \text{(III)}$$

or its reactive derivative at the carboxy group or a salt thereof, wherein R^1 is defined above, to give a compound of formula (I).

40. A pharmaceutical composition which comprises, as an active ingredient, a compound of claim 37, or a pharmaceutically acceptable salt thereof in admixture with a pharmaceutically acceptable carrier or excipient.

41. A method for the therapeutic treatment of infectious diseases caused by pathogenic microorganisms, comprising administering an effective amount of a compound of claim 37 or a pharmaceutically acceptable salt thereof, to a human being or animal.--

REMARKS

Claims 37-41 are active in the application.

This case is a CPA of application serial No. 08/089723, in which a declaration was filed pursuant to 37 C.F.R. §1.132. The major issue in that case concerned whether the claims were commensurate in scope with data showing superior antifungal properties. The present claims are narrower, being directed to compounds in which R^1 is benzoyl substituted with a heterocycle which is itself substituted by phenyl having an alkoxy substitutent. These claims are commensurate in scope with data in the previously filed Rule 132 Declaration and the one submitted herewith (unexecuted) with data on the compound of Example 25 (claim 38).

Applicants submit that the case is now in condition for allowance. Early notification of such action is earnestly solicited.

Respectfully submitted,

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